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Epidemiological Profile, Risk Factors, and Clinical Outcomes of Neonatal Candidemia in a Tertiary Care Hospital, Jammu, India

Shalu Mengi*, Ojasvi Sharma and Sandeep Dogra

Department of Microbiology, GMC Jammu, India

**Corresponding author*

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A B S T R A C T

Neonatal candidemia is an emerging cause of bloodstream infections in Neonatal Intensive Care Units (NICUs), particularly among preterm and low birth weight infants. This study aimed to determine the prevalence, species distribution, and associated risk factors of neonatal candidemia in a tertiary care hospital in North India. A hospital-based observational study was conducted over one year (August 2024–July 2025) at Government Medical College, Jammu, in collaboration with the NICUs of Shri Maharaja Gulab Singh Hospital. A total of 4,520 neonates were screened. Blood samples were collected under strict aseptic precautions and processed using conventional culture techniques. Candida isolates were identified by germ tube test, CHROMagar Candida, and sugar fermentation and assimilation tests. Clinical and demographic data were analyzed using SPSS, with $p < 0.05$ considered statistically significant. Ninety-eight cases of candidemia were identified. Male predominance was observed (68.9%), with most cases occurring within the first 10 days of life. Low birth weight (75.5%) and prematurity (74.4%) were common. Universal prior exposure to broad-spectrum antibiotics was noted. Non-albicans Candida species predominated (93.8%), with *Candida tropicalis* emerging as the most frequent isolate. Additional risk factors included intravenous cannulation and ventilator support. Neonatal candidemia in this setting is strongly associated with prematurity, low birth weight, invasive interventions, and prior antibiotic exposure. The predominance of non-albicans Candida, particularly *C. tropicalis*, underscores an evolving epidemiological trend. Strengthening antimicrobial stewardship and infection control practices is essential to reduce morbidity and improve neonatal outcomes.

Introduction

Candidemia, defined as the isolation of *Candida* species from the bloodstream, represents the most common manifestation of invasive candidiasis and is a major cause of morbidity and mortality among hospitalized patients worldwide. It accounts for more than 90% of fungal bloodstream infections and remains a significant challenge in intensive care units (ICUs), particularly among neonates and immunocompromised individuals (Pappas *et al.,* 2018; Kotey *et al.,* 2021).

Although *Candida albicans* has historically been the predominant etiological agent, there has been a marked epidemiological shift over the past decade toward non-albicans *Candida* (NAC) species, including *Candida*

tropicalis, *Candida glabrata*, and *Candida parapsilosis* (Lamoth *et al.,* 2018; Friedman *et al.,* 2019).

The distribution of *Candida* species varies geographically. In North America and Australia, *C. glabrata* is increasingly prevalent, whereas *C. tropicalis* predominates in India and Pakistan. In Europe, *C. albicans* still accounts for the majority of cases, though NAC species collectively represent a substantial and growing proportion of infections (Galia *et al.,* 2022; Ray *et al.,* 2022). This epidemiological transition is attributed partly to widespread azole use, particularly fluconazole, which has exerted selective pressure favoring intrinsically less susceptible NAC species (Pappas *et al.,* 2018). The unpredictable antifungal susceptibility patterns of these species pose significant therapeutic challenges and contribute to adverse clinical outcomes (Friedman *et al.,* 2019).

The pathogenicity of *Candida* species is mediated by multiple virulence determinants. Adhesion to host tissues represents a critical initial step in infection. Members of the agglutinin-like sequence (ALS) family, particularly Als3 in *C. albicans*, facilitate adherence to epithelial and endothelial cells and promote endocytosis via interaction with host cadherins. NAC species possess distinct adhesins, such as Epa proteins in *C. glabrata*, which contribute to colonization and biofilm development (Ciurea *et al.,* 2020). Hydrolytic enzymes, including secreted aspartyl proteinases (SAPs), phospholipases, and lipases, further enhance tissue invasion and immune evasion. Although SAP activity is more pronounced in *C. albicans*, *C. tropicalis* demonstrates significant proteolytic activity associated with disseminated infections (Malinovska *et al.,* 2023).

Morphological and genomic plasticity further augment fungal adaptability. The ability of *Candida* species to transition between yeast, pseudohyphal, and hyphal forms alters cell wall architecture and immune recognition. Genomic rearrangements and mutations enhance survival under antifungal stress, contributing to drug resistance (Ciurea *et al.,* 2020). The fungal cell wall, composed of an inner polysaccharide matrix (β-glucans, mannans, and chitin) and an outer protein layer containing pathogen-associated molecular patterns (PAMPs), plays a pivotal role in host–pathogen interaction. Increased chitin content has been linked to reduced antifungal penetration and resistance development (Hassan *et al.,* 2021).

Neonates, particularly those born prematurely or with low birth weight (LBW), represent a highly vulnerable population. Immaturity of innate and adaptive immune responses—including reduced neutrophil function, incomplete development of pattern recognition receptors (PRRs), and impaired Th17-mediated immunity—predisposes them to invasive fungal infections (Michalski *et al.,* 2017). The absence of protective vernix caseosa, disruption of epithelial barriers due to invasive procedures, prolonged ICU stay, and broad-spectrum antibiotic exposure further increase susceptibility (Weimer *et al.,* 2022). Antibiotic-induced depletion of commensal gut flora removes protective anti-*Candida* mechanisms, promoting fungal overgrowth and systemic dissemination (Pappas *et al.,* 2018).

Globally, the incidence of candidemia ranges from 2–14 cases per 100,000 population, with substantially higher rates in developing countries and ICU settings. In India, candidemia accounts for a significant proportion of bloodstream infections, with an incidence of approximately 6.5 per 1000 ICU admissions, and NAC species—particularly *C. tropicalis*—predominate (Ray *et al.,* 2022; Mathur *et al.,* 2022). Mortality remains high, especially among neonates, where invasive candidiasis is associated with long-term neurodevelopmental sequelae, including cerebral palsy, cognitive impairment, and sensory deficits (Pana *et al.,* 2017).

The rising incidence of NAC species, increasing antifungal resistance, and high mortality among vulnerable populations underscore the need for accurate species identification and timely antifungal susceptibility testing. Understanding evolving epidemiological patterns and virulence mechanisms is essential for improving therapeutic strategies and clinical outcomes in candidemia. This study aims to determine the prevalence of candidemia among neonates admitted to the Neonatal Intensive Care Unit (NICU), to identify and characterize the Candida species isolated from bloodstream infections in this population, and to evaluate the associated clinical and epidemiological risk factors contributing to the isolation of Candida species in NICU-admitted neonates.

Materials and Methods

Study Design and Setting

This hospital-based observational study was conducted in the Department of Microbiology, Government Medical College (GMC), Jammu, in collaboration with the Neonatal Intensive Care Units (NICUs) of Shri Maharaja

Gulab Singh Hospital (SMGSH), Jammu. The study was designed to evaluate the prevalence, species distribution, and associated risk factors of neonatal candidemia in a tertiary care setting catering to high-risk neonates, including preterm and low birth weight infants.

Ethical clearance was obtained from the Institutional Ethics Committee (IEC) of Government Medical College, Jammu, prior to commencement of the study. All procedures were conducted in accordance with institutional ethical guidelines and the principles of the Declaration of Helsinki. Confidentiality of patient data was strictly maintained throughout the study period.

Sample Size

The calculated sample size was 4,520 neonates. The estimation was based on an anticipated prevalence (p) of 3% derived from previous epidemiological data (Caggiano *et al.,* 2017), with a margin of error of 0.53%, alpha level of 0.05, and beta of 0.2 (power = 80%), using OpenEpi software version 3. Adequate sample size calculation ensured sufficient statistical power to detect significant associations between candidemia and potential risk factors.

Study Period

The study was conducted over a one-year period, from 1st August 2024 to 31st July 2025. All blood samples were collected from neonates admitted to the NICUs of SMGSH, Jammu, during this timeframe. Both inborn and outborn neonates requiring intensive care support were included in the study population.

Sample Collection

Blood samples were collected under strict aseptic precautions to minimize contamination, in accordance with standard microbiological guidelines (Pappas *et al.,* 2018). Approximately a 5 cm diameter area over the venipuncture site was disinfected sequentially with 70% ethyl or isopropyl alcohol followed by 10% povidone-iodine solution. The site was allowed to air dry for at least one minute before venipuncture to ensure adequate antisepsis. Approximately 1 mL of peripheral venous blood was collected from each neonate and inoculated immediately into Brain Heart Infusion (BHI) broth for conventional culture. Blood was collected exclusively from peripheral veins and not from pre-existing intravenous catheters to avoid false-positive results due to catheter colonization. The volume collected adhered to neonatal blood culture recommendations to optimize pathogen recovery while minimizing blood loss in this vulnerable population (Thomas-Rüddel *et al.,* 2022).

Transport and Storage

All inoculated BHI broth bottles were properly labeled and accompanied by requisition forms containing demographic and clinical details. Samples were transported to the Department of Microbiology as early as possible. In cases of unavoidable delay, specimens were maintained at room temperature to preserve viability, as recommended for fungal blood culture processing (CLSI guidelines). Timely transport and processing were prioritized to improve isolation rates and reduce contamination risk.

Sample Processing and Identification

Upon receipt in the laboratory, blood samples in BHI broth were subcultured onto two Sabouraud Dextrose Agar (SDA) slopes and incubated at 25°C and 37°C to enhance fungal recovery and morphological differentiation. After overnight incubation, colonies were examined for characteristic creamy, smooth, pasty, and convex morphology suggestive of *Candida* species.

Gram staining of colony smears was performed to identify budding yeast cells and pseudohyphae. Species-level identification was carried out using conventional phenotypic methods, including: Germ tube test, CHROMagar Candida differential media, Sugar fermentation tests and Sugar assimilation tests. The use of CHROMagar Candida allowed preliminary differentiation based on colony pigmentation patterns, improving diagnostic accuracy and turnaround time (Galia *et al.,* 2022). Identification methods were aligned with standard mycological diagnostic practices (Pappas *et al.,* 2018).

Data Collection

Clinical and demographic data were obtained from requisition forms and patient medical records. The variables recorded included age, sex, birth weight, gestational age, history of ventilator support or intubation, presence of intravenous cannulation, use of broad-spectrum antibiotics, and duration of NICU stay.

These variables were selected based on established risk factors for neonatal candidemia reported in recent literature (Weimer *et al.,* 2022; Ray *et al.,* 2022). Particular emphasis was placed on prematurity and low birth weight due to their strong association with invasive fungal infections.

Statistical Analysis

All collected data were systematically entered into Microsoft Excel and subsequently analyzed using the Statistical Package for the Social Sciences (SPSS), latest available version. Qualitative variables were summarized as frequencies and percentages, while quantitative variables were expressed as mean ± standard deviation (SD). Associations between categorical variables were evaluated using the Chi-square test. A two-tailed p-value of < 0.05 was considered statistically significant for all analyses.

Results and Discussion

Prevalence of Neonatal Candidemia

During the study period from 1 August 2024 to 31 July 2025, a total of 4,520 blood samples from neonates admitted to the NICUs of SMGS Hospital, Jammu, were processed in the Department of Microbiology, Government Medical College (GMC) Jammu. Candida species were isolated from 98 samples, yielding an overall prevalence of 2.16%. Blood samples were collected aseptically (1 mL) from a peripheral vein and inoculated into Brain Heart Infusion (BHI) broth bottles for conventional culture. Bottles were appropriately labeled and accompanied by duly completed requisition forms prior to laboratory processing.

This prevalence is higher than that reported by Kaur *et al.,* (2020), who documented a prevalence of 1.31% in a similar tertiary care setting.

Distribution of *Candida* Species

Following standard microbiological identification and speciation procedures, including subculture on Sabouraud Dextrose Agar (SDA) and CHROMagar, the species distribution was determined. Non-*albicans Candida* (NAC) species accounted for 92 (93.8%) of cases. *Candida tropicalis* was the predominant isolate (63.2%**),** followed by *Candida glabrata* **(**22.3%**).** *Candida albicans* accounted for only 6.1% of cases. *Candida parapsilosis* and *Candida krusei* were isolated in 5.1% and 3.0% of cases, respectively. On CHROMagar, steel blue colonies (65.3%) were most commonly observed after overnight incubation at 37°C, consistent with the predominance of *C. tropicalis*. Distinct colony coloration facilitated preliminary differentiation of species.

Clinical Profile of Neonates with Candidemia

Gender Distribution

Among the 98 neonates with candidemia, 66 (68.9%) were males and 32 (31.1%) were females, yielding a male-to-female ratio of 2.2:1.

Age Distribution

The majority of cases (38.7%) occurred in neonates aged 1–5 days, followed by 30.6% in the 6–10 day age group. Fewer cases were observed in older neonates, with only 2.2% occurring in the 26–30 day age group.

Birth Weight Distribution

Low birth weight (LBW; <2500 g) was observed in 75.5% of the neonates. Among them, 43.8% weighed between 1500–2500 g, 32.2% were classified as very low birth weight (VLBW; <1500 g), and 3.3% were extremely low birth weight (ELBW; <1000 g). Only 24.4% of neonates had a normal birth weight (≥2500 g).

Table.1 Distribution of Candida species causing candidemia

Candida species	N	%
Candida tropicalis	62	63.2
Candida glabrata	22	22.4
Candida albicans	6	6.1
Candida parapsilosis	5	5.1
Candida krusei	3	3.0
	98	

Table.2 Gender distribution among neonates

Gender	N	%
Male	66	67.3
Female	32	32.6

Total	98	100

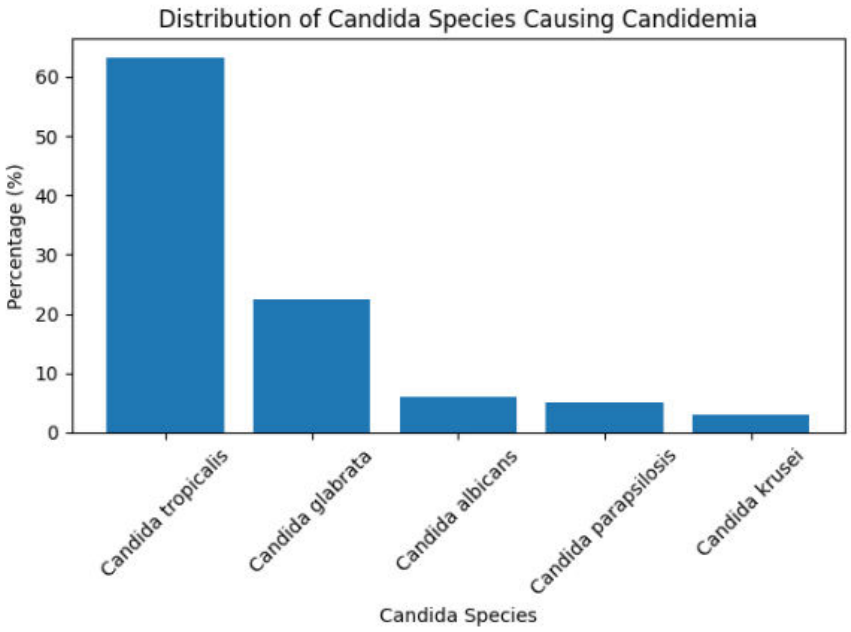

Table.3 Age- wise distribution of neonates

Age (in days)	N	%
1-5	38	38.7
6-10	30	30.6
11-15	14	14.2
16-20	9	9.1
21-25	5	5.1
26-30	2	2.0
Total	98	

Table.4 Birth weight (in grams) wise distribution of neonates

Birth weight (in grams)	N	%
>_2500 g	24	24.4
<2500 g - 1500 g	43	43.8
<1500 g - 1000 g	28	28.5
<1000 g	3	3.3
Total	98	

Table.5 Cause of admission of neonates

Cause of admission	N	%
Respiratory distress	66	67.3
NNH	13	13.2
Feed intolerance	11	11.2
Congenital anomalies	4	4.4
Bacterial sepsis	4	4.4
Total	98	100

Table.6 Risk factors associated with neonatal candidemia

Risk factor	N	%
Prior antibiotic usage	98	100
IV cannulation	98	100
LBW	69	75.6
Preterm birth	68	74.4
Male gender	63	68.9
Mechanical ventilation/intubation	32	35.6

These findings indicate that the majority of admitted neonates were vulnerable due to suboptimal birth weight, which may have contributed to increased morbidity and susceptibility to infections.

Cause of Admission

Respiratory distress was the most common cause of NICU admission, accounting for 67.3% of cases, followed by icterus (13.2%) and feed intolerance (11.2%). Congenital anomalies and bacterial sepsis each contributed to 4.4% of admissions. The predominance of respiratory distress highlights the critical need for early respiratory support and intensive monitoring in this population.

Risk Factors Associated with Neonatal Candidemia

The most frequently identified risk factors associated with neonatal candidemia included prior broad-spectrum antibiotic usage (100%), intravenous cannulation, low birth weight (75.6%), preterm birth (74.4%), male gender (68.9%), and ventilator support (35.6%). The universal exposure to broad-spectrum antibiotics underscores its significant role in predisposing neonates to fungal infections. Additionally, invasive procedures and prematurity further increased the vulnerability of these neonates to candidemia, emphasizing the importance of strict infection control practices and judicious antibiotic use in NICU settings.

Fungal bloodstream infections (BSIs) in neonates are predominantly caused by *Candida* species, particularly in NICU settings where invasive procedures and prolonged hospitalization are common (Sharma *et al.,* 2023). The increasing survival of preterm and low birth weight infants has contributed to the rising burden of neonatal candidemia.

In the present study, NAC species predominated (93.8%), with *Candida tropicalis* emerging as the most common isolate. This finding is consistent with several recent Indian studies. Biswas *et al.,* (2023) reported *C. tropicalis* as the predominant isolate in a teaching hospital in Jharkhand. Similar observations were made by Kardam *et al.,* (2023) in Uttar Pradesh and by Lamba *et al.,* (2021). Basu *et al.,* (2017) and Yadav *et al.,* (2017) also documented a predominance of *C. tropicalis* in neonatal candidemia cases in tertiary care centers in Central India and Haryana, respectively. The predominance of NAC species reflects a shifting epidemiological trend, possibly attributable to selective antifungal pressure and widespread empirical antibiotic usage.

Prior antibiotic exposure was identified as a universal risk factor in the present study. Comparable findings have been reported by Baby *et al.,* (2021) and Koppad *et al.,* (2017), who identified previous antibiotic use as a major risk factor in neonatal candidemia. In a multicenter Indian study, Chakrabarti *et al.,* (2020) similarly identified broad-spectrum antibiotic use as the most significant predisposing factor. Furthermore, Cook *et al.,* (2023) reported that 85% of neonates with candidemia in low- and middle-income countries had received broad-spectrum antibiotics.

Antibiotic administration disrupts the normal gastrointestinal microbiota, diminishing bacterial competition and facilitating fungal overgrowth (Esaiassen *et al.,* 2017). The gut microbiota normally suppresses fungal proliferation through nutrient competition and production of antifungal metabolites. Broad-spectrum antibiotics alter this balance, increasing susceptibility to invasive candidiasis.

This effect is particularly pronounced in preterm neonates, whose gut microbiota diversity is already

limited and further compromised following antibiotic exposure (Ventin-Holmberg *et al.,* 2022).
Low birth weight and prematurity were also strongly associated with candidemia in the present study. Immature immune responses, prolonged hospital stay, invasive interventions, and frequent antibiotic exposure collectively increase susceptibility in this population.

Overall, the findings highlight the growing importance of NAC species, particularly *Candida tropicalis*, in neonatal candidemia and emphasize the need for antimicrobial stewardship and strict infection control practices in NICUs.

In conclusion, the present study highlights the significant burden of neonatal candidemia in the NICU, predominantly affecting preterm and low birth weight infants. A clear male predominance and early onset within the first week of life were observed. Non-albicans Candida species, particularly *Candida tropicalis*, emerged as the leading etiological agents, reflecting an evolving epidemiological shift. Universal exposure to broad-spectrum antibiotics and frequent invasive interventions were major predisposing factors. These findings underscore the urgent need for robust antimicrobial stewardship, stringent infection control practices, and early risk stratification strategies to reduce morbidity and improve clinical outcomes in this highly vulnerable neonatal population.

Author Contributions

Shalu Mengi: Investigation, formal analysis, writing—original draft. Ojasvi Sharma: Validation, methodology, writing—reviewing. Sandeep Dogra:—Formal analysis, writing—review and editing.

Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethical Approval Not applicable.

Consent to Participate Not applicable.

Consent to Publish Not applicable.

Conflict of Interest The authors declare no competing interests.

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