# Predictors of candidemia in pediatric patients (0–12 years) admitted in a tertiary care hospital of Northern India

**Sourabh Kumar[1], Ratan Gupta[2], Malini R Capoor[3], Sugandha Arya[4], Amitabh Singh[5]**

*From [1]Senior Resident, [2]Associate Professor, [4]Professor, [5]Assistant Professor, Department of Pediatrics, [3]Professor, Department of Microbiology, Vardhman Mahavir Medical and Safdarjung Hospital, New Delhi, India*

**Correspondence to:** Dr. Ratan Gupta, Department of Pediatrics, Vardhman Mahavir Medical and Safdarjung Hospital, New Delhi - 110 029, India. E-mail: ratangupta100@yahoo.com

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## ABSTRACT

**Background:** Bloodstream infections due to *Candida* species are becoming a major cause of morbidity and mortality in hospitalized patients. The emergence of non-*albicans Candida* (NACs) species with lesser susceptibility to antifungals has added to the woes of clinicians. **Objectives:** The objectives of the study were to determine the clinical and laboratory predictors and microbiological profile of candidemia in pediatric patients. **Materials and Methods:** This is a hospital-based, prospective, and cross-sectional study conducted in the pediatric department of a tertiary care hospital. A total of 250 children aged 0–12 years with risk factors for fungal sepsis were enrolled. Demographic details, clinical, and laboratory parameters were noted and samples were sent for culture. Cultures yielding growth of *Candida* were included in the study, and antifungal susceptibility performed. Associations were assessed using Chi-square test first and then through logistic regression models. **Results:** Among the 250 patients with risk factors for fungal sepsis, 47 patients (18.8%) with culture proven candidemia were identified. Predictors of candidemia among neonates were prematurity (<30 weeks), prolonged ventilation (>72 h), and thrombocytopenia. Among pediatric patients, prolonged steroid intake, *Candida* isolation from sites other than blood and persistent neutropenia, were significantly associated with the candidemia. NAC species were the predominant isolates (78.7%). **Conclusion:** Candidemia should be suspected in premature neonates requiring prolonged ventilation with unexplained thrombocytopenia. Among pediatric patients, prolonged steroid intake, *Candida* isolation from sites other than blood and persistent neutropenia are predictors of candidemia.

**Key words:** *Antifungals, Candidemia, Neonates, Predictors*

Candidemia has become the fourth most common bloodstream infection over the past two decades and is the leading cause of invasive fungal infections among hospitalized patients [1,2]. Fungal infections possess the second-highest case fatality rate (13%) among all causes of sepsis in children [3]. Pediatric patients who are diagnosed with candidemia have higher rates of mortality, increased length of hospital stay and a mean increase in total per patient hospital charges [4]. The prevalence of infections caused by non-*albicans Candida* (NAC) species that may have less susceptibility to antifungal agents, has increased steadily, accounting for >50% episodes of candidemia in many surveys conducted in adults and children all over the world [5-9]. A myriad number of risk factors and predictors are associated with candidemia [10-17].

Only a few Indian studies have analyzed the cases of candidemia in pediatric patients prospectively. The primary objective of this study was to determine the predictors of candidemia in the pediatric population (0–12 years) admitted in a tertiary care hospital and the secondary objectives were to determine the clinical and microbiological profile and outcome of candidemia in these children.

## MATERIALS AND METHODS

This is a prospective, hospital-based study over a period of 1 year performed in a tertiary care hospital in New Delhi. The study was conducted after obtaining Institutional Ethics Committee's approval. The sample size was calculated taking the prevalence of suspected fungal sepsis among pediatric patients of 20% from the hospital registry. Children of 0–12 years with risk factors for fungal sepsis (which included prematurity, mechanical ventilation, urinary catheterization, recent surgery, and prolonged antibiotic therapy, hematological disorders, neutropenia, malnourishment, HIV-AIDS, prolonged steroid therapy, previous exposure to antifungals, and *Candida* isolation from sites other than blood or sterile body fluids) were tracked from the admission register of the wards. Patients with risk factors for fungal sepsis and who remained sick even after 72 h of treatment with broad-spectrum antibiotics or had strong suspicion of fungal sepsis based on their underlying disease condition were enrolled in the study after taking consent from the parents. Presenting clinical features and results of laboratory investigations (including serial hemograms, absolute neutrophil counts (ANCs), blood chemistries, liver and

**Table 1: Bivariate and multivariate association between risk factors and candidemia in neonates**

| Variables | Crude OR (95% CI) | p values | Adjusted OR (95% CI) | p value |
|---|---|---|---|---|
| Prematurity (<37 weeks) | | | | |
| <30 | Reference | - | Reference | |
| 30–34 | 0.2 (0.07–0.64) | 0.006 | 0.13 (0.03–0.6) | **0.009** |
| 34–37 | - | - | - | - |
| Mechanical ventilation | | | | |
| None | Reference | | Reference | |
| <72 h | 0.78 (0.19–3.25) | 0.737 | 0.25 (0.02–2.54) | 0.239 |
| >72 h | 6.47 (1.92–21.75) | 0.003 | 8.62 (1.91–39) | **0.005** |
| Neutropenia | | | | |
| No | Reference | | Reference | |
| Yes | 1.16 (0.29–4.7) | 0.83 | 2.91 (0.45-18.78) | 0.262 |
| Prolonged antibiotic therapy | | | | |
| None | Reference | | Reference | |
| <72 h | 0.85 (0.22–3.24) | 0.808 | - | |
| >72 h | - | - | - | |
| Recent surgery (within last 2 weeks) | | | | |
| No | Reference | | Reference | |
| Yes | - | - | - | - |
| Urinary catheterization | | | | |
| None | Reference | | Reference | |
| >72 h | - | - | 0.00 (0.00–0.00) | 0.999 |
| *Candida* isolation from other sites | | | | |
| No | Reference | | Reference | |
| Yes | - | - | 0.00 (0.00–0.00) | 0.998 |

**OR: Odds ratio, CI: Confidence interval**

kidney function tests, Gram stain and culture from appropriate body fluids, and C-reactive protein only for neonates) were recorded serially.

Five ml blood sample was withdrawn from the enrolled patients under strict aseptic precautions in the biphasic medium using Brain Heart Infusion Agar and broth and sent for fungal blood culture. Other sterile fluids for fungal culture (e.g., cerebrospinal fluid [CSF], peritoneal or pericardial fluid) were sent in sterile culture bottles. Urine for fungal hyphae and culture was sent simultaneously with the fungal blood culture to assess *Candida* isolation from sites other than blood and sterile body fluids. Samples were processed the same day or if delay was anticipated then the samples were stored at 2–8°C. The biphasic medium was incubated at 37°C for 48 h. *Candida* growth was identified based on their morphology on Corn Meal Agar, HiCrome agar, germ tube test, and ascospore production on malt extract agar, growth at 42°C, and cycloheximide tolerance. In case of unusual isolates, DNA sequencing was done at Mycology Referral Centre, PGIMER, Chandigarh. Antifungal susceptibility testing was done by broth microdilution, and E-strip method and interpretation were done as per CLSI M27 A3, 2012, and CLSI M44A [18].

The diagnosis of candidemia was done as per the EORTC/Mycoses Study Group consensus group criteria [19]. The consensus group defines proven invasive fungal disease (IFD) as the demonstration of fungal elements on histopathologic, cytopathologic, or direct microscopic examination of a biopsy specimen or recovery of fungal elements from the culture of blood or a sterile body fluid under proper sterile conditions. Probable IFD requires the presence of a host factor, a clinical criterion, and mycological evidence of fungal infection. Cases that meet the criteria for a host factor and a clinical criterion but for which mycological criterion are absent is considered possible IFD. (In this study, we have taken only proven cases of candidemia in whom a *Candida* species was isolated on culturing blood or a sterile body fluid obtained under aseptic precautions).

Children with risk factors for fungal sepsis and whose fungal culture revealed the growth of *Candida* species were taken as cases and children with risk factors for fungal sepsis but whose fungal culture showed no growth were taken as the control group. Children with risk factors for fungal sepsis and whose fungal culture revealed the growth of organisms other than *Candida* were excluded from the study.

The diagnosed cases were managed as per the existing standard unit policy, guided by the culture and sensitivity reports. Children were followed until discharge or death. Parameters of morbidity included starting of feeds after initiation of treatment (among neonates) and duration of stay in the hospital. The outcome was taken as whether the child got discharged or did not survive.

The diagnosed cases were analyzed for the underlying risk factors, presenting clinical features and laboratory outcomes, and the results were compared with the control group to assess the clinical and laboratory predictors of candidemia in pediatric patients. Since the clinical profile, risk factors and the laboratory studies done in the neonatal and pediatric groups were quite different, we analyzed the neonatal and pediatric groups, separately. There were a lot of confounding factors in predictors of candidemia, so we used logistic analysis to nullify the effect of confounding factors among the predictors of candidemia.

Chi-square test was used to determine the association of clinical features, lab parameters, and risk factors between candidemia patients and non-candidemia patients. Multiple logistic regression models were used to test these associations adjusting for all other variables that may work as confounding factors. The results were considered significant at 5% level of significance. All the analyses were done using statistical software SPSS 17.0.

## RESULTS

During the study period, 302 children aged 0–12 years having risk factors for fungal sepsis and meeting the inclusion criteria were enrolled in the study. Out of these, 52 children were excluded from the study as 7 children grew fungi other than *Candida*

**Table 2: Bivariate and multivariate association between laboratory parameters and candidemia among neonates**

| Variables | Crude OR (95% CI) | p value | Adjusted OR (95% CI) | p value |
|---|---|---|---|---|
| Absolute neutrophil count 1 | | | | |
| >1500/mm$^3$ | Reference | | Reference | |
| 1000–1500/mm$^3$ | 1.37 (0.13–14.03) | 0.789 | - | - |
| 500–1000/mm$^3$ | 1.37 (0.13–14.03) | 0.789 | - | - |
| <500/mm$^3$ | - | - | - | - |
| Absolute neutrophil count 2 | | | | |
| >1500/mm$^3$ | Reference | | Reference | |
| 1000–1500/mm$^3$ | - | - | - | - |
| 500–1000/mm$^3$ | 1.5 (0.36–6.3) | 0.58 | - | - |
| <500/mm$^3$ | 4 (0.24–67.47) | 0.336 | - | - |
| Absolute neutrophil count 3 | | | | |
| >1500/mm$^3$ | Reference | | Reference | |
| 1000–1500/mm$^3$ | 3.09 (0.63–15.22) | 0.165 | - | - |
| 500–1000/mm$^3$ | - | - | - | - |
| <500/mm$^3$ | 2.06 (0.18–24.18) | 0.564 | - | - |
| Liver function tests | | | | |
| N | Reference | | Reference | |
| abN | - | - | - | - |
| Kidney function tests | | | | |
| N | Reference | | Reference | |
| abN | 1.3 (0.24–6.97) | 0.762 | - | 0.996 |
| Serum electrolytes | | | | |
| N | Reference | | Reference | |
| abN | 4.11 (0.54–31.19) | 0.172 | 95,000,000 (0–0) | 0.995 |
| Platelet count | | | | |
| N for age | Reference | | Reference | |
| ↓ for age | 2.85 (1.02–7.96) | **0.046** | 4.47 (0.96–20.76) | 0.056 |
| C-reactive protein | | | | |
| NA | Reference | | Reference | |
| Negative | 0.55 (0.07–4.56) | 0.576 | 0.63 (0.1–3.89) | 0.617 |
| Positive | 0.49 (0.08–2.94) | 0.437 | - | - |
| CSF study | | | | |
| NA | Reference | | Reference | |
| N | 0.36 (0.06–2.35) | 0.289 | 0.44 (0.02–10.28) | 0.612 |
| abN | 0.5 (0.03–8.95) | 0.638 | - | - |

**CSF: Cerebrospinal fluid, OR: Odds ratio, CI: Confidence interval**

species in their fungal blood culture (1 *Histoplasma* spp., 3 *Trichosporon* spp., and 3 *Aspergillus* spp.), and the rest had incomplete data or they left against medical advice. Hence, a total of 250 children were analyzed in our study.

Among the 250 patients, 47 patients (18.8%) with culture proven candidemia caused by a single species were identified as cases, and the rest 203 were in the control group. Among these, 43 cases grew *Candida* spp. in blood while the rest grew *Candida* spp. in sterile body fluids (1 in CSF, 1 in pericardial fluid, and 2 in peritoneal fluid).

Of the total 250 children analyzed in the study, 57.6% of children were males. There were 38.4% neonates (<1 month) and rest were pediatric patients (1 month–12 years). The median postnatal age of the neonates was 21 days while the median age of pediatric patients was 5 years. The mean gestational age of neonatal patients was 31.2±2.1 weeks, and the mean birth weight was 1.25±0.24 kg.

The case and control groups were matched for age and sex. However, there was a significant difference in the mean gestational age and birth weight in the two groups among neonates. The mean gestational age was 29.85±1.53 weeks among cases and 31.5±2.11 weeks among controls ($p<0.05$). Similarly, the mean birth weight was 1.12±0.16 kg and 1.28±0.25 kg among cases and controls, respectively ($p<0.05$).

More than one-third of patients were neonates with sepsis and meningitis. The next largest group was of patients with hematological disorders (ALL and other hematological malignancies and aplastic anemia), who accounted for 18.4% (n=46) of the study population. Other patients enrolled were having pyrexia of unknown origin/septicemia (32, 12.8%),

**Table 3: Bivariate and multivariate association between risk factors and candidemia among pediatric patients**

| Variables | Crude OR (95% CI) | p values | Adjusted OR (95% CI) | p value |
|---|---|---|---|---|
| Mechanical ventilation | | | | |
| Others | Reference | | Reference | |
| <72 h | - | - | - | - |
| >72 h | 1.7 (0.42–6.9) | 0.456 | 9664.09 (4.68–20,000,000) | 0.018 |
| Hematological disorders | | | | |
| No | Reference | | Reference | |
| Yes | 2.44 (1.04–5.71) | 0.039 | 33.61 (0.5–2279.23) | 0.102 |
| Neutropenia | | | | |
| No | Reference | | Reference | |
| Yes | 2.17 (0.93–5.06) | 0.072 | 0.07 (0–5.64) | 0.233 |
| Malnourishment | | | | |
| None | Reference | | Reference | |
| Moderate | 0.3 (0.04–2.45) | 0.263 | 0.06 (0–2.04) | 0.119 |
| Severe | 0.52 (0.14–1.87) | 0.314 | 0.69 (0.1–4.86) | 0.713 |
| Prolonged steroids (>2 weeks) | | | | |
| None | Reference | | Reference | |
| Yes | 2.26 (0.9–5.67) | 0.082 | 5.91 (1.5–23.26) | **0.011** |
| Prolonged antibiotics therapy | | | | |
| None | Reference | | Reference | |
| <72 h | - | | 1 (0–0) | 0 |
| >72 h | 0.69 (0.13–3.75) | 0.665 | 3.29 (0.13–84.9) | 0.472 |
| Previous antifungal therapy | | | | |
| No | Reference | | Reference | |
| Yes | 4.75 (1.82–12.38) | 0.001 | 3.87 (0.92–16.38) | 0.066 |
| Recent surgery (within past 2 weeks) | | | | |
| No | Reference | | Reference | |
| Yes | 10.08 (0.88–115.48) | 0.063 | 8.89 (0.42–188.88) | 0.161 |
| Urinary catheterization | | | | |
| None | Reference | | Reference | |
| <72 h | 0.65 (0.08–5.49) | 0.689 | 0.01 (0–1.44) | 0.071 |
| >72 h | 0.65 (0.08–5.49) | 0.689 | 0.0004 (0–1.07) | 0.052 |
| HIV-AIDS | | | | |
| No | Reference | | Reference | |
| Yes | - | - | - | - |
| *Candida* isolation from other site | | | | |
| No | Reference | | Reference | |
| Yes | 3.62 (1.5–8.75) | 0.004 | 11.92 (2.84–50) | **0.001** |

**OR: Odds ratio, CI: Confidence interval**

protein-energy malnutrition (24, 9.6%), nephrotic syndrome (19, 7.6%), primary immunodeficiency or HIV-AIDS (4, 1.6%), post-surgical cases (4, 1.6%), and others (26, 10.4%). No significant association was seen between cases of candidemia and the underlying diseases. Similarly, there was no significant difference in the clinical presentation of the case and control groups in both neonatal and pediatric populations.

Among the risk factors, 100% neonates were premature. About 43.75% neonates required ventilation (26.04% required ventilation <72 h while 17.7% required ventilation >72 h). Neutropenia was present in 13.54% neonates. About 93.75% neonates had received prolonged antibiotics >72 h, but none were exposed to antifungals, previously. Only 5.2% neonates had history of recent surgery, and only 4.1% were catheterized for >72 h. *Candida* was isolated from a site other than blood or sterile body fluids in 5.2% neonates.

Among neonates, in multivariate logistic regression analysis, only extreme prematurity (gestation <30 week) and prolonged ventilation (>72 h) were significantly associated with the study group (Table 1). Neonates who were 30–34 weeks premature were 87% less likely to be in the study group than neonates who were <30 weeks premature (odds ratio [OR]=0.13, p=0.009). Similarly, neonates with >72 h ventilation were 8.62 times more likely to be in the study group than neonates with no ventilation (OR=8.62, p=0.009).

Among the lab parameters, only thrombocytopenia had a significant association with candidemia in neonates (Table 2). Platelet count reduced for age was present in 65% of neonates in the case group as compared to 39.5% neonates in the control group (p<0.05). In multiple logistic regression, this association also lost the significance (p=0.056), though the neonates with decreased platelet count were 4.47 times more likely to be in the case group (OR=4.47) than the neonates with normal for age platelet counts after adjusting other laboratory parameters.

In pediatric patients, among the risk factors, mechanical ventilation was required in 13.6%, the hematological abnormality was present in 31.2% patients while neutropenia was present in 33.1% of patients. About 32.5% of patients were malnourished, 20.7% of patients had history of prolonged steroid intake, and 75.3% of patients had received antibiotics for >72 h. About 15.6% of patients were previously exposed to antifungals. HIV-AIDS was present in 1.3% patients, 1.95% of patients had a history of recent surgery and 5.2% of patients had history of urinary catheterization for >72 h. *Candida* was isolated from sites other than blood or sterile body fluids in 22.72% patients.

After adjusting for all the confounding factors only prolonged steroid use (>2 weeks) and *Candida* isolation from a site other than blood or sterile body fluids were (Table 3) significantly associated with candidemia in pediatric patients. Pediatric patients with prolonged steroid use were 5.91 times more likely to be in the study group after adjusting other risk factors (OR=5.91, p=0.011). Furthermore, pediatric patients with *Candida* isolation from other sites were 11.92 times more likely to be in the study

**Table 4: Species wise sensitivity pattern**

| Species (total no of isolates) | A | | F | | V | |
|---|---|---|---|---|---|---|
| | N | % | N | % | N | % |
| *Candida albicans* (10) | 10 | 100 | 7 | 70 | 10 | 100 |
| *Candida parapsilosis* (14) | 14 | 100 | 11 | 78.57 | 14 | 100 |
| *Candida tropicalis* (11) | 10 | 90.9 | 6 | 54.54 | 10 | 90.9 |
| *Candida glabrata* (7) | 4 | 57.1 | 2 | 28.6 | 7 | 100 |
| *Candida krusei* (2) | 2 | 100 | 0 | 0 | 2 | 100 |
| *Candida guilliermondii* (1) | 0 | 0 | 0 | 0 | 1 | 100 |
| *Candida auris* (2) | 0 | 0 | 0 | 0 | 2 | 100 |

A=Amphotericin B, F=Fluconazole, V=Voriconazole

group (OR=11.92, p=0.001). Although prolonged ventilation was also significantly associated with the study group (p=0.018), the OR was not reliable (OR=9664).

Among laboratory parameters, ANC <1500/mm$^3$ was significantly associated with candidemia in pediatric patients. Pediatric patients with 500–1000/mm$^3$ value in ANC1 were 4.72 times more likely to be in the case group than the pediatric patients with >1500/mm$^3$ (p=0.004). Furthermore, pediatric patients with <500/mm$^3$ value in ANC2 were significantly 3.55 times more likely to be in the case group than the neonates with >1500/mm$^3$ (p=0.008). In multiple logistic regression analysis however these associations lapsed due to not having sufficient values to estimate ORs.

The species of *Candida* growth among cases of prevalence are shown in Fig. 1. *Candida parapsilosis* was the most common species among neonates (13 out of 20, 65%) and *Candida tropicalis* was the most common species among pediatric cases (10 out of 27, 37%).

A total of 36% of patients that were enrolled in the study died while rest were discharged. Mortality among the candidemia cases was 42.6% while the rest 57.4% were discharged. Similarly, among the control group, 34.5% of patients died while 65.5% were discharged. However, no significant difference was seen between the cases and controls with respect to outcome in terms of discharge or death.

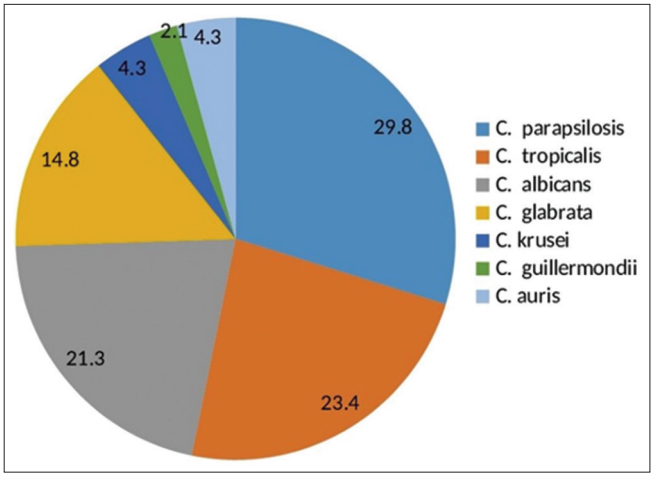


**Figure 1: *Candida* species isolated in the study population**

## DISCUSSION

The species distribution of *Candida* species among study cohort showed that *Candida albicans* constituted 21.3% of cases while NACs constituted 78.7% cases. This was in accordance with recent studies in Indian setups which also confirmed a similar predominance of NACs with isolation rates ranging from 66% to 90% [20-23].

The most frequent isolate in our study was *C. parapsilosis* (29.8%) which was predominantly found among neonatal cases. Xess *et al*. [24] also found a shift of predominant species to *C. parapsilosis* in patients of all ages. This advent of *C. parapsilosis* in neonatal cases in India is alarming as it is an exogenous pathogen that may be found on the skin and is quite notorious for the ability to form biofilm on catheters and other implanted devices, for nosocomial spread by hand carriage, and for persistence in the hospital environment [25]. Most of the infections are acquired in association with intravascular catheters and parenteral nutrition. Thus, the detection of *C. parapsilosis* BSI should be a "red flag" regarding breaks in catheter care and infection control procedures.

In the present study, the sensitivity pattern of the growths revealed that fluconazole resistance was seen in 44.68% cases, and amphotericin-B resistance was seen in 14.9% cases, and only one isolate was resistant to voriconazole (Table 4). While most of *C. albicans* (70%) and *C. parapsilosis* (78.57%) isolates were sensitive to fluconazole, fluconazole sensitivity was only 54.54% among *C. tropicalis* isolates and only 28.6% among *Candida glabrata* spp. This was in contrast to the previous study conducted in the year 2004 in the same hospital by Capoor *et al*. [18] that showed only 4.9% and 6.9% resistance to fluconazole and amphotericin-B, respectively. This increase in resistance to fluconazole and amphotericin-B might be explained by the changes in the treatment policy of the hospital where use of antifungal prophylaxis in children of hematological malignancies with febrile neutropenia has increased rampantly.

The study shows that neonates with gestational age <30 weeks were more likely to have candidemia as compared to neonates with 30–34 weeks. Furthermore, neonates with prolonged ventilation (>72 h) were more likely to have candidemia as compared to the reference population with no mechanical ventilation. Similar results were found in many studies in Indian setups as well as

abroad [26-28]. Extreme prematurity is a well-established risk factor for candidemia. The immature immune system, higher mean intensive care unit stay with exposure to nosocomial fungal infections, increased requirement of invasive procedures such as mechanical ventilation, central and peripheral venous lines, and prolonged total parenteral nutrition, and antibiotic requirement all might contribute to increased risk of candidemia in premature neonates.

Among laboratory parameters, thrombocytopenia emerged as the major laboratory predictor in neonates. It is a well-known concept that preterm babies with low birth weight have a limited response to thrombocytopenia in terms of platelet production and thrombopoietin [29]. This response might become limited during an episode of sepsis where the host has decreased energy reserves and possibly hepatic injury [30]. Many studies have been done among neonates to study the association between neonatal sepsis and platelet count, and it was found that the incidence of thrombocytopenia was highest among cases of fungemia and these cases were associated with greater decrease in platelet count from the baseline as compared to Gram-positive and Gram-negative sepsis [31]. Bhat *et al*. showed the association of thrombocytopenia with Gram-negative sepsis and candidemia and concluded that mortality increased in the group of neonates with candidemia and thrombocytopenia as compared to neonates with candidemia but no thrombocytopenia (36% vs. 16%) [32]. Thus, unexplained thrombocytopenia in preterm neonates with sepsis should raise the suspicion of candidemia, and the neonate should be aggressively investigated and managed for the same as the outcome might be poorer.

*Candida* isolation from sites other than blood and sterile body fluids, which has an adjusted OR of 11.92 (p=0.001) emerged as a strong predictor of candidemia in pediatric patients. Although we only screened urine for fungal hyphae and *Candida* species growth and in rare cases skin scrapings, endotracheal secretions or sputum for *Candida* isolation from other sites, the results were quite significant. Urine culture reports from candidemia cases showed that 29.6% (8 out of 27) pediatric cases of candidemia had simultaneous candiduria. The overall incidence of candiduria among candidemia cases was 21.27%. Chakrabarti *et al*. had a similar observation in their study where they found that candiduria was more likely a predictor of disseminated infection in patients having non-*albicans candidemia* [33].

Furthermore, prolonged steroid use (>2 weeks) emerged as a major risk factor among pediatric patients with an adjusted OR of 5.91 (p=0.011). Prolonged steroid use (>2 mg/kg/day for >2 weeks) is an established risk factor for candidemia in adults [34].

The results of the bivariate analysis showed that patients with hematological disorders were 2.44 times more likely to be associated with candidemia (p=0.039). Similarly, patients with previous exposure to antifungal treatment were 4.75 times more likely to have candidemia (p=0.004). However, they lost their significance on adjusting for other confounding factors in multivariate analysis. Although these are established risk factors for candidemia, caution must be exercised while declaring them as predictors of candidemia because of the increased chances of bias. The demographic profile of our study population showed that the most predominant group among pediatric patients is of hematological disorders, many of whom are started on prophylactic antifungal therapy in view of their neutropenic status. Thus, further studies with appropriately matched study cohorts and larger sample size are required to explore their role as predictors of candidemia.

Among pediatric patients, low ANC came out as the most significant laboratory predictor of candidemia. Neutropenia is a well-established risk factor of candidemia [35]. Blyth *et al.* in their study found that among cases of candidemia, children were more likely to have neutropenia as compared to neonates and adults [27].

The outcome in the present study was measured in terms of duration of hospital stay and mortality, and no significant difference was seen among the case and control groups with regard to these measures. Mortality was comparable in both the groups (34.5% in candidemia cases and 42.6% in control patients). In this study, mortality attributable to candidemia could not be found as there are no clear cut measures to attribute the mortality to candidemia and also because of the serious underlying disease process in both case and control groups which might have confounded the outcome. Thus, it is only by matched cohort studies we can study the excess mortality and morbidity attributable to candidemia.

## CONCLUSION

In this study, it was inferred that extreme prematurity (<30 weeks), prolonged ventilation (>72 h), and thrombocytopenia are strong predictors for candidemia in neonates while prolonged steroid intake (>14 days), *Candida* isolation from sites other than blood, and neutropenia (ANC<1000) are strong predictors for candidemia in pediatric patients in our setup.

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