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Original Research Article

CLINICAL PROFILE AND DETERMINANTS OF CANDIDAL SEPSIS IN NEONATES: A RECORD-BASED DESCRIPTIVE STUDY IN A TERTIARY CARE HOSPITAL IN MANDYA

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ABSTRACT

Background: Candida bloodstream infections (BSIs) are a significant and increasing cause of neonatal sepsis and related mortality, particularly in preterm and low-birth-weight neonates. The similarity in presentation between bacterial and fungal infections often leads to diagnostic delays. This study aimed to evaluate the clinical profile, maternal and neonatal risk factors, and antimicrobial resistance patterns in neonates with candidemia admitted to a tertiary NICU. The objective is to describe maternal and neonatal factors associated with candidemia and to analyze the clinical profile, morbidity, mortality, and antifungal sensitivity patterns in affected neonates.

Materials and Methods: A retrospective descriptive study was conducted from January 2022 to January 2024 at the NICU of Mandya Institute of Medical Sciences, Karnataka. Medical records of 80 neonates with blood culture-proven Candida infection were reviewed. Demographic, clinical, and laboratory data were analyzed. Species identification and antifungal sensitivity testing were performed. Statistical analysis included chi-square and unpaired t-tests, with significance set at $p<0.05$.

Results: Candidemia accounted for 28% of all neonatal sepsis cases. Most cases (77.5%) presented as early-onset sepsis (<72 hours), and 75% were outborn. Risk factors included low birth weight (particularly 1500–2500 g), preterm birth, pre-labor rupture of membranes, maternal antibiotic use, and prolonged labor. Candida albicans accounted for 77% of infections, while non-albicans species comprised 23%. A history of umbilical vein catheterisation was present in 46.5% of subjects, with C. albicans being more frequently identified in this group (19.4% vs 0%, $p=0.002$). Non-albicans infections were associated with longer hospitalization (>21 days, $p=0.024$), higher rates of intraventricular haemorrhage ($p<0.001$), severe thrombocytopenia ($p=0.01$), convulsions, shock, and feed intolerance. Only 43.4% of isolates were sensitive to fluconazole, whereas 88.2% were sensitive to voriconazole and 51.2% to amphotericin B. Non-albicans species showed significantly higher sensitivity to amphotericin ($p=0.041$).

Conclusion: Candidemia is an emerging and serious contributor to neonatal sepsis in India, associated with substantial morbidity and antifungal resistance. Early identification of risk factors and awareness of local epidemiological patterns are crucial to guide preventive strategies and appropriate antimicrobial therapy. Rising fluconazole resistance, especially among non-albicans Candida, underscores the importance of species-specific management and antimicrobial stewardship.

Keywords: Neonatal candidemia; Candida albicans; Non-albicans Candida; Neonatal sepsis; Antifungal resistance.

INTRODUCTION

Candida bloodstream infection (BSI) is an important cause of neonatal sepsis and sepsis-related mortality in newborns.[1] The cumulative incidence is <0.3% among infants weighing >2500 g, but it increases to about 8% in those weighing <750 g. Candida species are the third most common cause of bloodstream infections in infants and are estimated to account for 2–4% of early-onset neonatal sepsis and 10–12% of late-onset neonatal sepsis.[2]

Candida BSI is defined as at least one pure growth of Candida species in a blood culture within 72 hours of inoculation.[3] It typically presents with clinical features suggestive of sepsis, including respiratory distress or apnea, tachycardia or bradycardia, poor perfusion, feeding intolerance, temperature instability, lethargy, or seizures.[4]

The incidence of candidiasis in neonatal intensive care units (NICUs) has risen steadily over the past two decades, paralleling improved survival of premature newborns due to advances in intensive care.[5] Preterm, very low birth weight (<1500 g), extremely low birth weight (<1000 g), and critically ill infants are at the highest risk due to their immature immune systems, invasive interventions, and prolonged use of antimicrobials. Additional risk factors for fungal infection include the use of H2 blockers, steroids, aminophylline, prior colonization, central venous catheters, prolonged use of broad-spectrum antibiotics, total parenteral nutrition, and extended NICU stay.[6]

Candida BSI is associated with 25–40% mortality and with end-organ damage in the brain, heart, kidneys, and eyes in up to 73% of cases.[7] Mortality reaches 40% in infants <750 g and 20% in those weighing 1000–1500 g.[8] Survivors often suffer long-term neurological impairment, including cerebral palsy, blindness, hearing impairment, and cognitive deficits.

Fungal colonization of the skin, gastrointestinal tract, and respiratory mucosa occurs in 26.7% to 62.5% of critically ill neonates within the first two weeks of life. Candida species may be transmitted vertically from maternal flora or horizontally from healthcare workers.[6]

Fungal infections have emerged as a significant cause of neonatal late-onset sepsis in the past two decades. Because the clinical presentation of invasive fungal infections closely resembles that of bacterial sepsis, delays in diagnosis and treatment are common. Given the high mortality and difficulty of early diagnosis, it is crucial to identify risk factors for invasive candidiasis and to understand its clinical presentation and impact on morbidity and mortality.[9]

Objectives

The objectives of this study were:

1. To describe the maternal and neonatal factors associated with candidemia in neonates admitted to the NICU at Mandya Institute of Medical Sciences, Mandya.
2. To describe the clinical profile, morbidity, and mortality patterns in these neonates.

MATERIALS AND METHODS

A record-based descriptive study was conducted over a two-year period (January 2022 to January 2024) among 81 neonates admitted to the Neonatal Intensive Care Unit (NICU) of a tertiary care teaching hospital (Mandya Institute of Medical Sciences, Mandya, Karnataka) after obtaining clearance from the institutional ethics committee.

The sample size was determined by purposive sampling, based on the proportion of candidemia among all cases of neonatal sepsis in the NICU. All neonates admitted with a positive blood culture for Candida species were included. Neonates who left against medical advice or whose case records were incomplete and unavailable for full follow-up were excluded.

As per institutional NICU protocol, blood culture was sent for all babies presenting with features of sepsis or any episode of clinical deterioration. Cultures were performed by conventional methods: 5 ml of blood was collected in Brain Heart Infusion broth and plated on MacConkey agar and blood agar every 48 hours until growth was detected. Species identification was performed by biochemical testing. Cultures were reported as negative if no growth was observed after 7 days.

The demographic and clinical profiles of both mother and neonate were recorded using a predesigned extraction sheet. Case records were analyzed for risk factors including sex, gestational age, birth weight, mode of delivery, duration of hospital stay, antibiotic exposure, use of total parenteral nutrition, H2-blocker or steroid use, and presence of indwelling central venous catheters. Clinical features assessed included feeding intolerance, temperature instability, apnea/respiratory distress, hypo- or hyperglycemia, type of respiratory support required, shock, convulsions, thrombocytopenia, and the need for blood or blood product transfusion. Morbidity and mortality parameters such as duration of hospitalization and duration of mechanical ventilation were documented. Culture and sensitivity patterns were noted, and comparisons were drawn.

Data Analysis: Data were entered in Microsoft Excel and analyzed using SPSS trial version software. Descriptive statistics (percentage and proportion for categorical variables such as sex, gestational age, premature rupture of membranes, and thrombocytopenia; mean ± standard deviation for continuous variables such as age, birth weight, and duration of mechanical ventilation) were calculated. Inferential statistics included the chi-square test to assess associations between categorical variables (e.g., age, umbilical line catheterisation, foul-smelling liquor) and the unpaired t-test to compare means of continuous variables (e.g., birth weight, duration of hospitalization). A significance level of

5% (α=0.05) was used, with p<0.05 considered statistically significant.

RESULTS

Table 1: Distribution of maternal factors:

Maternal factors		Frequency (n=80)	Percent
Antenatal steroids	Yes	19	23.8
H/o maternal fever	Yes	14	17.5
H/O WDPV	Yes	30	37.5
Foul smelling discharge	Yes	78	97.5
H/O PROM	<12 hrs	23	28.7
	12-24 hrs	4	48.8
	>24 hrs	18	22.5
Antepartum use of antibiotics	Yes	42	52.5
H/o prolonged labour	12-24 Hr	60	75
	>24 Hr	20	25
Place of delivery	Inborn	20	25
	Outborn	60	75
Place of delivery	Government	76	95
	Private	4	5
Type of labour	Induced	37	46.3
	Spontaneous	43	53.8
Mode of delivery	Caesarean	39	48.8
	Vaginal	41	51.2

Table 2: Baseline Characteristics and neonatal clinical parameters of Study Population

	Total (n, %)	Candida albicans species (n, %)	Non- albicans candida (n, %)	p-value
Age at admission				0.634
<72 hr	62 (77.5)	48 (77.4)	10 (71.4)	
>72 hr	18 (22.5)	14 (22.6)	4 (28.6)	
Sex				0.146
Female	46 (57.5)	32 (51.6)	10 (71.4)	
Male	34 (42.5)	30 (48.4)	4 (28.6)	
Duration of hospitalisation (days)				0.024
<7	8 (10.0)	4 (6.5)	4 (6.5)	
7–14	18 (22.5)	18 (29.0)	0 (0)	
15–21	45 (56.3)	35 (56.5)	10 (71.4)	
>21	9 (11.3)	5 (8.1)	4 (28.6)	
Gestational age				0.124
Term	28 (35.0)	24 (38.7)	4 (28.6)	
Early preterm	17 (21.3)	11 (17.7)	6 (42.9)	
Late preterm	35 (43.8)	27 (43.5)	4 (28.6)	
Birth weight (grams)				0.017
1000–1500	25 (31.3)	19 (30.6)	6 (42.9)	
1500–2500	31 (38.8)	19 (30.6)	8 (57.1)	
>2500	24 (30.0)	24 (38.7)	0 (0)	
Growth category (AGA/SGA/LGA)				0.618
AGA	42 (52.5)	34 (54.8)	8 (57.1)	
SGA	34 (42.5)	24 (38.7)	6 (42.9)	
LGA	4 (5.0)	4 (6.5)	0 (0)	
Assisted ventilation				0.093
CPAP	40 (50.0)	36 (58.1)	4 (28.6)	
Mechanical ventilation	18 (22.5)	12 (19.4)	6 (42.9)	
O_2	14 (17.5)	10 (16.1)	4 (28.6)	
Duration of CPAP (hours)				0.248
<24	28 (38.9)	16 (25.8)	6 (42.9)	
24–48	37 (51.3)	39 (62.9)	8 (57.1)	
>72	7 (9.7)	7 (11.3)	0 (0)	
Frequent phlebotomies/peripheral line changes (>3/week)				0.187
Present	73 (91.3)	55 (88.7)	14 (100)	
Duration of umbilical vein catheterisation (days)				0.002
<7	25 (31.3)	15 (24.2)	10 (71.4)	
>7	12 (15.0)	12 (19.4)	0 (0)	

Table 3: Clinical Manifestations of Study Population

Clinical Manifestations	Total (n=80)	Candida albicans (n, %)	Non-albicans candida (n, %)	p-value
Lethargy	67 (83.8)	53 (85.5)	14 (100)	0.129
Feed intolerance	47 (58.8)	37 (59.7)	10 (71.4)	0.026
Convulsions	34 (42.5)	24 (38.7)	10 (71.4)	0.026
Shock	34 (42.5)	24 (38.7)	10 (71.4)	0.026
NEC	6 (7.5)	6 (9.7)	0 (0)	0.225
IVH	4 (5.0)	0 (0)	4 (28.6)	<0.001
Bleeding manifestations	18 (22.5)	18 (29.0)	0 (0)	0.021
Thrombocytopenia				0.01
<50,000	14 (17.5)	8 (12.9)	6 (42.9)	
50,000–100,000	28 (35.0)	24 (38.7)	0 (0)	
>1 lakh	26 (32.5)	18 (29.0)	8 (57.1)	

Table 4: Distribution of drug sensitivity among candida and non candida group

Drug sensitivity		Cultured organism		Total	P value
		Candia albicans	Non candida-albicans		
Fluconazole	YES	29	4	33	0.215
		46.80%	28.60%	43.40%	
Voriconazole	YES	53	14	67	0.253
		85.5%	100%	88.20%	
Amphotericin	YES	30	11	41	0.041

DISCUSSION

Candida species have emerged as important pathogens causing neonatal sepsis in both India and worldwide. In this study, candidemia accounted for 28% of culture-proven sepsis cases, highlighting its rising significance. Identifying risk factors is essential for prevention and improved outcomes.[10]

The majority of neonates were outborn admissions, consistent with findings from other Indian studies. As most were referred within the first day of life, emphasis on hygienic antenatal and delivery practices in peripheral healthcare facilities is critical. Maternal factors commonly associated with candidemia included prolonged labor, premature rupture of membranes, and antepartum antibiotic use, while maternal fever was uncommon. Similar risk factors were reported by Wadile et al., where intrapartum antibiotic use, vaginal delivery, and low birth weight were associated with neonatal candidemia.[11,12]

In contrast to many studies that reported candidemia primarily as a cause of late-onset sepsis, most cases here were early-onset, suggesting intrapartum acquisition. Kumaravel et al. in Tamil Nadu, India, reported a 1.43% incidence, with 86% weighing <2.5 kg and 84% being preterm. Devleta et al. (2016–2018) reported similar risk factors in a study of 48 neonates with fungal sepsis. International studies (China, Italy, Brazil) also support extreme prematurity and very low birth weight as major risk factors. Interestingly, our study also found late preterm neonates (1500–2500 g) significantly affected.[13,14]

Clinical manifestations in our cohort were consistent with previous literature, including lethargy, feeding intolerance, convulsions, and shock. However, notable differences emerged: non-albicans Candida infections were associated with higher rates of IVH, severe thrombocytopenia, and prolonged hospitalization. These associations are less well described in prior studies and may warrant further exploration.[15]

Antifungal resistance patterns in our study reflect a growing concern. More than half of isolates were resistant to fluconazole, the first-line agent in our hospital. Amphotericin B retained activity, particularly against non-albicans Candida. Voriconazole showed the highest overall sensitivity. The rising prevalence of non-albicans Candida species and their resistance patterns mirror global trends, likely due to increasing empirical azole use. Similar findings were reported by Chen et al. in China and by Basu et al. in India.[16]

These results highlight the importance of local epidemiological surveillance, routine species identification, and susceptibility testing to guide therapy. They also emphasize the need for antimicrobial stewardship to curb inappropriate antifungal use.[17]

Limitations

This study was retrospective and limited to a single center, restricting the range of determinants assessed and the generalizability of findings. Larger, multicentric prospective studies are needed to confirm these associations and to better guide preventive and therapeutic strategies.

CONCLUSION

Candidemia is an important and rising cause of neonatal sepsis, associated with significant morbidity, mortality, and antifungal resistance. In this study, early-onset cases were strongly linked to maternal factors such as premature rupture of membranes, prolonged labor, and antibiotic use, as well as neonatal risk factors including prematurity, low birth weight, and invasive procedures. Non-albicans Candida species were associated with more severe complications, including intraventricular

hemorrhage, severe thrombocytopenia, convulsions, and prolonged hospitalization. The high prevalence of fluconazole resistance, with better sensitivity to voriconazole and amphotericin B, emphasizes the need for species-specific antifungal therapy and strict antimicrobial stewardship. Strengthening infection control during delivery and NICU care, improving diagnostic surveillance, and adopting evidence-based treatment protocols are essential to reduce the burden of neonatal candidemia and improve outcomes.

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