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A Study on Neonatal Candidemia in A Tertiary Care Hospital

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Abstract

Background : Neonatal candidemia is rapidly becoming one of the commonest causes of sepsis in NICUs. The speciation of Candida and the identification of the associated risk factors is pertinent for prevention and proper treatment of patients as most of the fluconazole resistant strains recovered from clinical specimens, particularly blood, are NAC species. **Material and Methods**: The study was an observational study carried out on 4235 blood samples were collected from neonates admitted to the NICUs of SMGSH Jammu over a period of 1year w.e.f. 1st August 2023 to 31st July 2024. **Results:** A total of 90/4235 (2.12%) of the neonatal blood samples tested positive for candidemia. Candida tropicalis (63.3%) was the commonest Candida species isolated followed by Candida glabrata (23.3%), Candida albicans (5.6%), Candida parapsilosis (4.4%) and Candida krusei (3.3%). Prior antibiotic usage (100%), IV cannulation (100%), preterm birth (74.4%), LBW (75.6%), male gender (68.9%), mechanical ventilation (35.6%), NVD (54.4%) and maternal risk factors (58.9%) were the associated risk factors. **Conclusion:** The present study is in concordance with the increasing worldwide trend of isolation of NAC species from the blood of neonates.

Keywords: Neonatal candidemia, Non-Albicans Candida

Introduction

The emergence of NAC species as an important cause of candidemia is a worldwide phenomenon and the species distribution varies according to the geographical location. In most Asian countries, Candida albicans is still the most commonly isolated species from blood followed by Candida tropicalis. Whereas in India and Pakistan, Candida tropicalis is the most commonly isolated species. [1]

The incidence of candidemia has increased five-fold worldwide in the last ten years. The incidence of candidemia worldwide ranges from 2-14 cases per 100,000 people and 6.87 per 1000 ICU patients. The rate of candidemia in developing countries is 4-15 times higher than in developed

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countries. In the pediatric ICU in developing countries, the incidence is 42.7 cases per 1000 admissions. The incidence in developing countries ranges from 0.026 to 4.2 cases per 1000 admissions. The incidence of candidemia in India is 6.51 per 1000 ICU admissions. [2,3]

Candida colonization, biofilm formation on medical devices such as mechanical ventilator, usage of broad-spectrum antibiotics, premature birth, low birth weight, are some of the several risk factors associated with candidemia. [4,5]

Methodology

Study Design and Setting

This observational study was conducted in the Department of Microbiology, Government Medical College, Jammu, J&K over a period of 1 year, i.e., from 1st August 2023 to 31st July 2024. This study was conducted after obtaining clearance and permission from Institutional Ethical Committee (IEC) of Government Medical College, Jammu.

Study Population

All the consecutive first blood culture of neonates admitted in the NICU of SMGSH were included for a period of one year.

The present study was conducted on blood samples collected from the neonates admitted in the NICUs of SMGSH, Jammu from 1st August 2023 to 31st July 2024. About 1 ml of blood was collected from each neonate, inoculated into the BHI broth bottle and sent for microbiological examination to the Department of Microbiology, GMC Jammu. All the blood samples were collected from a peripheral vein and not from pre-existing intravenous catheter.

All the bottles were transported to the laboratory as early as possible and if there was a delay in transport, the bottles were kept at room temperature.

The blood samples in BHI broth were inoculated onto two SDA slopes and incubated at 25 degrees Celsius and 37 degrees Celsius overnight for culture. After overnight culture, gram staining was performed on the smear prepared from the colonies to see the presence of yeast and pseudohyphae of Candida species. Speciation of the isolates was done by conventional methods including Germ tube test, CHROMagar Candida test media, Sugar fermentation and assimilation tests.

Data Collection

For the determination of associated risk factors, data collection including age, sex, birth weight, gestational history and history of ventilator support or intubation, intravenous cannulation and use of broad-spectrum antibiotics was done from the requisition forms provided with each blood sample.

All the collected data was entered in the Excel Sheet and was analysed by using statistical software. The qualitative variables were reported as frequencies and percentages and the quantitative variables were reported as mean and standard deviation. Relationship between different variables

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was tested by Chi Square Test. A P value of <0.05 was considered as significant. All P values were two-tailed.

Results

Candida species were isolated from 90 out of total 4235 blood samples of neonates sent to The Department of Microbiology, GMC Jammu for microbiological examination. The overall prevalence of candidemia among neonates admitted to the NICUs of SMGSH, Jammu from 1st August 2023 to 31st July 2024 was calculated as 2.12%.

NAC species were isolated from 85 (94.4%) cases of neonatal candidemia. Candida tropicalis (63.3%) was the most commonly isolated species followed by Candida glabrata (23.3%) and Candida albicans (5.5%). Candida parapsilosis was isolated from 4 (4.4%) neonates and Candida krusei was isolated from only 3 (3.3%) neonates **(Table 1).**

Prior antibiotic usage and IV cannulation were the most commonly associated risk factors with neonatal candidemia followed by LBW (75.6%) and preterm birth (74.4%). Males (68.9%) were more predisposed than females (31.1%). 35.6% were on ventilator support **(Table 2).**

53 (58.9%) out of 90 neonates with candidemia had mothers with an underlying disease with hypothyroidism (25.6%) being the commonest one followed by GDM (24.4%). Less common clinical conditions included PROM, APH , Pre-eclampsia and allergic cough **(Table 3).**

The p value (<0.05) is significant, so, there is association between gestational age and the candida species isolated from the blood of neonates.
Candida tropicalis (45.6%) is most commonly isolated from neonates in the gestational age range of 32-36 weeks. 61.9% isolates of Candida glabrata were isolated from neonates in the gestational age range of 32-36 weeks. 60% isolates of Candida albicans were isolated from neonates born before 32 weeks of gestation. 66.7% isolates of Candida krusei were isolated from neonates born at or after 37 weeks of gestation. Candida parapsilosis was isolated from preterm and term neonates. **(Table 4)**

The comparison between sugar fermentation test and sugar assimilation test with respect to CHROMagar shows that the former is more sensitive than the latter. The diagnostic accuracy of sugar fermentation test (91.4%) is more than that of sugar assimilation test (83.7%). **[Table 5 and 6]**

Discussion

Fungal BSIs in neonates are caused mainly by Candida species. Neonates admitted to the NICUs are at particular risk because of the increased chances of survival due to the intensive care provided to them. NAC species are increasingly becoming an important cause of candidemia in neonates, especially those that are in the NICUs. Various factors that predispose a neonate to Candida BSIs include prematurity of birth, LBW, prior use of antibiotics and medical devices.[6]

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 11, 2024

In the present study, the prevalence of candidemia in the neonates admitted to the NICUs of SMGS hospital in Jammu for the stated study period was 2.12%. Kaur H *et al*.[7] reported a prevalence of 1.31%.

In the present study, Candida tropicalis was the most commonly isolated species of Candida. Out of 90 cases of neonatal candidemia, Candida tropicalis was isolated from the blood of 57 (63.3%) neonates. Biswas B *et al*.[8] also predominantly isolated Candida tropicalis from the blood of neonates in a teaching hospital in Jharkhand. In another study in Uttar Pradesh, Candida tropicalis was the most common species of Candida isolated from the blood of neonates by Kardam V *et al*.[9] On the contrary, Pandita N *et al*.[10] predominantly isolated Candida glabrata (54%) from the blood of neonates admitted to the NICU of a hospital in Uttarakhand.
In the present study, prior antibiotic usage was the risk factor common to all the neonates. Similar results were obtained by Baby *et al*.[11] in a study conducted on neonatal candidemia at a tertiary care hospital in North India. Similar results were obtained by Koppad B *et al*.[12] in a study conducted in Karnataka.

In the present study, 74.4% neonates with candidemia were preterm and 75.6% were LBW. Nazir A *et al*.[13]in a similar study conducted in Kashmir found that preterm birth and LBW were the most significant risks for neonatal candidemia.

In the present study, among 90 neonates positive for Candida species blood culture, 62 (68.9%) were males and 28 (31.1%) were females. Similar results were obtained by Radi NAAM *et al*.[14]

In the present study, mechanical ventilation played a role as a risk factor. 35.6% of the neonates with candidemia were on ventilator support. Similar results were obtained in a study conducted by Lakra SS *et al*.[15]

In the present study, 54.4% of the affected neonates were born vaginally. Vaginal delivery promotes colonization with Candida species implicating route of delivery as a risk factor.[16]
In the present study, 58.9% of the neonates with candidemia had mothers with an underlying disease with hypothyroidism (25.6%) and GDM (24.4%) being the commonest. The endocrinological and metabolic changes including GDM during pregnancy can cause significant alterations in the vaginal microbiome and predispose the neonate to infections caused by Candida species.[17]
The present study highlights a statistically significant association between gestational age and the Candida species isolated from the blood of neonates. There are distinct patterns of Candida species isolation based on the neonates' gestational age. Specifically, Candida tropicalis and Candida glabrata were predominantly isolated from preterm neonates born between 32 and 36 weeks, whereas Candida albicans was most commonly found in those born before 32 weeks of gestation. Conversely, Candida krusei was predominantly isolated from term neonates, while Candida parapsilosis was observed across both preterm and term groups.
In the present study, the comparison between sugar fermentation test and sugar assimilation test with respect to CHROMagar showed that the diagnostic accuracy of sugar fermentation test (91.4%) was more than that of sugar assimilation test (83.7%). The sensitivity of sugar

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 11, 2024

fermentation test was 95.6% whereas that of sugar assimilation test was 91.1%. Giri S *et al*.[18] came to a similar conclusion.

Conclusion

The present study highlights the need to perform speciation of the Candida isolates from neonatal blood as there is an increasing worldwide trend of isolation of Non-albicans Candida (NAC) species from blood samples especially from the ICUs. The associated risk factors should be kept in mind during inpatient management and antifungal drugs should be prescribed accordingly as many NAC species show intrinsic resistance to antifungal drugs.

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ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 11, 2024

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Table 1: Distribution of Candida species causing candidemia

Candida species	N (%)
Candida tropicalis	57 (63.3)
Candida glabrata	21(23.3)
Candida albicans	5(5.6)
Candida parapsilosis	4(4.4)
Candida krusei	3(3.3)

Table 2: Risk factors associated with neonatal candidemia

Risk factor	N (%)
Prior antibiotic usage	90 (100)
IV cannulation	90 (100)
LBW	68 (75.6)
Preterm birth	67 (74.4)
Male gender	62 (68.9)
Mechanical ventilation/intubation	32 (35.6)
NVD	49 (54.4)

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 11, 2024

Table 3: Maternal risk factors

Risk Factor	N(%)
Hypothyroidism	23(25.6)
GDM	22(24.4)
PROM	4(4.4)
APH	2(2.2)
Pre-eclampsia	1(1.1)
Allergic cough	1(1.1)
None	37(41.1)
Total	90(100)

Table 4: Gestational age (in weeks) and Candida species wise distribution of neonates

Gestational age (in weeks)	Candida species												P Value
	Candida tropicalis		Candida glabrata		Candida albicans		Candida parapsilosis		Candida krusei		Total		
	n	%	n	%	n	%	n	%	N	%	N	%	
>_ 37 weeks	15	26.3	3	14.3	2	40	1	25	2	66.7	23	25.6	0.016
32-36 weeks	26	45.6	13	61.9	0	0	1	25	0	0	40	44.4	

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 11, 2024

<32-28 weeks	15	26.3	4	19.0	2	40	1	25	1	33.3	23	25.6	
<28 weeks	1	1.76	1	4.8	1	20	1	25	0	0	4	4.4	
Total	57	100	21	100	5	100	4	100	3	100	90	100	

Table 5: Comparison between Sugar Fermentation Test and CHROMagar

Sugar Fermentation Test	**CHROMagar**		**Total**
	Positive	Negative	
Positive	86	4	90
Negative	4	0	4
Total	90	4	94

Table 6: Comparison between Sugar Assimilation Test and CHROMagar

Sugar Assimilation Test	**CHROMagar**		**Total**
	Positive	Negative	
Positive	82	8	90
Negative	8	0	8
Total	90	8	98