Original Research Article

Assessment of the prevalence of nonalbicans candidemia in neonates and their antifungal susceptibility pattern- A Cross-sectional Study

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Abstract

Background: Candida species are known to be the most common fungal pathogens isolated from blood cultures of neonates. Recent reports from our country indicates trend towards an increasing prevalence of non-albicans candidemia. Candida species possess a number of virulence factors which enable them to cause hematogenously disseminated infections in susceptible hosts with increased morbidity and mortality. **Aim:** The aim of current study was to assess the prevalence of nonalbicans candidemia in neonates and their antifungal susceptibility pattern. **Methods:** Blood samples from suspected cases of neonatal septicaemia were subjected to culture, incubated for 7 days and subcultures performed. Culture yielding pure growth of Candida were included for the study and identified by standard methodology. Antifungal susceptibility was performed. **Results:** A total of 255/500 (51%) cases were blood culture positive. Pure growth of Candida species was isolated from 52/255 (20.39%) cases. A total of 52 Candida isolates were obtained over a period of one year accounting for 20.39% of all neonatal septicemia cases. Among 52 isolates, 14/52 (26.92%) were Candida albicans, followed by C. tropicalis 19/52 (36.53%), C. glabrata 10/52 (19.23%), C. parapsilosis 4/52 (7.69%), C. guillermondii 2/52 (3.84%) and C. krusei 1/52 (1.92%). C. tropicalis, the most common species isolated, was 91 per cent susceptible to fluconazole, whereas C. parapsilosis and C. glabrata showed lower sensitivity rates of 67.8% and 62.5% respectively. **Conclusion:** In this study non albicans candida was the common isolate & they showed decreased resistance to Fluconazole**.** In neonatal septicemia speciation& antifungal susceptibility may help in management.

Keywords: Candidemia, mycosis, Fluconazole.

Introduction

The frequency of invasive, opportunistic mycosis has increased significantly over the past two decades. Candida species account for 8-10% of all nosocomial blood stream infections[1]. Candidemia is a significant cause of mortality and morbidity in neonates admitted in the Neonatal Intensive Care Units (NICUs)[2]. Candida species are the most common fungal pathogen isolated from the blood culture of neonates. A number of risk factors are associated with the development of neonatal systemic candidiasis, such as low-birth weight babies, prematurity, prolonged antibiotic therapy, parenteral nutrition and artificial ventilation[3].Respiratory insufficiency, apnoea, bradycardia, temperature instability, feeding intolerance and abdominal distension are the various clinical manifestations associated with candidiasis[4]. Prompt treatment with antifungals is required in these babies. Limited data regarding the pattern of neonatal candidemia from this part of the country prompted us to undertake the present study to assess the changing trend of neonatal candidemia. The aim of present study is to evaluate the prevalence of candidemia in neonates and to assess the changing trends of candidemia in neonates.

Methods

This Cross sectional observational, descriptive epidemiological study was conducted at Department of Paediatrics, at Vardhman Institute of Medical Sciences, Pawapuri, Nalanda, Bihar.

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The study was approved by the institutional research and ethical committee. The study was conducted between June 2020 and December 2020. An informed and written consent was taken from the participating subjects prior to the commencement of the study. Candidemia was diagnosed by isolation of Candida spp. from at least two blood culture samples or at least one positive blood culture containing pure growth of Candida species with supportive clinical features. This prospective study was conducted over one year from NICU of tertiary care institutes.A total of 500 blood samples of clinically diagnosed septicemic neonates were collected before starting antimicrobial therapy. The blood sample inoculated in the BacT/ALERT 3D pediatric culture bottle was incubated in an automated microbial detection system (bioMerieux) for up to 5 days at 37°C. Any growth indicated was subcultured on sheep blood agar, Mac Conkey agar plates and Sabouraud dextrose agar slant with antibiotics but without cycloheximide (Hi-Media Pvt. Ltd., Mumbai, India). Identification was performed using API ID32C (bioMerieux, France).Antifungal susceptibility testing was performed against amphotericin B (AMB), 5 flucytosine (5FC), fluconazole (FLU) and itraconazole(ITR) and voriconazole(VOR) by broth microdilution using API system [ATB FUNGUS 3 (259 isolates), bioMerieux, France]. Results were interpreted as per the Clinical Laboratory Standards Institute (CLSI; formerly NCCLS) M27-A2 document [5,6].

The data was tabulated and was subjected to statistical analysis using SPSS Software version 16.0.

Results

A total of 255/500 (51%) cases were blood culture positive. Pure growth of Candida species was isolated from 52/255 (20.39%) cases.

A total of 52 Candida isolates were obtained over a period of one year accounting for 20.39% of all neonatal septicemia cases. Of the 52 isolates, 14/52 (26.92%) were Candida albicans, followed by C. tropicalis 19/52 (36.53%), C. glabrata 10/52 (19.23%), C. parapsilosis 4/52 (7.69%), C. guillermondii 2/52 (3.84%) and C. krusei 1/52 (1.92%). Certain predisposing factors are associated with candidemia in present study as in Table 1.

Table 1: Potential risk factors identified in cases of neonatal candidemia (n=52)

Present Risk factors	No. of cases	Percentage
Prolonged IV antibiotics	52	100%
Low birth weight	32	61.53%
Prematurity	16	30.76%
Prolonged central venous line	21	40.38%
Ventilatory support	12	23.07%
Corticosteroid therapy	9	17.3%

In present study all 52 cases had history of administration of broad spectrum antibiotics for variable period of time as an important predisposing factor.

Other factors of importance are low birth weight, prematurity, catheterization & corticosteroid therapy etc.

Non candida albicans species, especially C. tropicalis, C. krusei, C. glabrata and C. parapsilosis, tend to be less- susceptible to azoles, particularly fluconazole, than C. albicans. C. krusei is innately resistant to fluconazole.

Studies have also revealed an inherent fluconazole resistance in C. glabrata thus emphasizing the need to identify Candida up to the species level, especially in the high-risk population.

Table 2 enumerates the antifungal resistance pattern of candida species.

C. tropicalis, the most common species isolated, was 91 per cent susceptible to fluconazole, whereas C. parapsilosis and C. glabrata showed lower sensitivity rates of 67.8% and 62.5% respectively.

Table 2: MIC profile of Candida isolates to amphotericin B and % sensitivity to other antifungals tested

Organism	Amphotericin B MIC <1 µg/ml	Flucytosine	Fluconazole	Itraconazole	Voriconazole
C .albicans	100	100	100	95	100
C. tropicalis	100	92	91	56	95.5
C. glabarata	100	100	62.5	21	84.5
C. parapsilosis	100	91.5	67.8	65.6	90.6
C. guillermondii	100	100	69	53	100
C. krusei	88.8	10.8	0	0	100

Discussion

There are varied reports regarding the prevalence of C. albicans and non-albicans Candida in bloodstream infections from the Indian sub-continent. As per the initial reports, most cases of neonatal candi-demia were caused by Candida albicans[1].

But in our study, C. tropicalis (36.53%) to be the major etiological agent. Our report is in concordance with other reports[2-4].

In present study prolonged IV antibiotics is most important predisposing factor associated with candidemia followed by other factors like low birth weight, prolonged central venous line etc. In the current study, amphotericin B (100%) was the most effective antifungal agent. In India, amphotericin B is the drug of choice for invasive candidiasis with low or no resistance reports[3].Our susceptibility data showed that reduced susceptibility to fluconazole was common in C. glabrata and C. parapsilosis. Reduced susceptibility to fluconazole in C. glabrata was consistent with previously reported data[7,8].Sarvikivi et al.[9] have reported that the use of fluconazole prophylaxis contributed to the emergence of subclones of C. parapsilosis with decreased susceptibility among isolates responsible for BSI in neonatal ICU. A significant epidemiological shift to higher isolation of non-albicans Candida species was noticed. The high usage of fluconazole appeared to have played a role in this shift, however, it may be recognised that other events like patient specific risk factors might have also contributed in selection of different species.

Conclusion

To conclude, our study highlights that within our country the epidemiology of neonatal candidemia differs markedly and therefore it is important for every setting to speciate and perform the antifungal susceptibility testing. This information will help us to recognize the emerging fungal pathogens and increasing drug resistance.

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