



RESEARCH ARTICLE

CANDIDEMIA IN A PEDIATRIC INTENSIVE CARE UNIT OF A TERTIARY CARE CENTRE

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ABSTRACT

**Background:** Candidemia is one of the most significant causes of morbidity and mortality in hospitalized neonates and pediatric patients especially in intensive care units.

**Objective:** The present study was planned to assess the prevalence of candidemia in neonatal and pediatric patients admitted to P.I.C.U.

**Method:** A cross-sectional prospective study was carried out in pediatric patients admitted to the P.I.C.U. of Sassoon General Hospital. A total of 485 blood samples from clinically suspected cases of blood stream infections of pediatric age group collected over six months were included in the present study. Candidemia was diagnosed by isolation of a pure culture of *Candida* spp. from at least one blood culture with supportive clinical features.

**Result:** From 485 clinically suspected cases of blood stream infections; a total of 5 (1.03%) cases were confirmed as candidemia. All the confirmed cases of candidemia were observed in neonates. Presence of intravascular catheter was the most common risk factor associated with all (100%) the cases followed by low birth weight (80%). Four (80%) cases of candidemia belonged to non-*albicans Candida*, whereas only one was caused by *Candida albicans*.

**Interpretation and Conclusion:** Prevalence of candidemia among clinically suspected cases of blood stream infections was 1.03%. All the confirmed cases of candidemia belonged to age group of 0 to 12 months. Presence of intravascular catheters was the most important risk factor followed by low birth weight. A shift observed in the etiological agents from *Candida albicans* to non-*albicans Candida*. It is important to identify the species as non-*albicans Candida* are more likely to be resistant to antifungal agents.

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INTRODUCTION

Blood stream infections are significant causes of morbidity and mortality in hospitalized patients especially in intensive care units (ICU). Blood stream infections (BSIs) caused by *Candida* species is known as candidemia (Wisplinhoff, 2004). Candidemia is defined as at least one blood culture positive for *Candida* species for a patient who developed signs or symptoms of BSI (Gudlaugsson, 2003). *Candida* species are the fourth commonest cause of blood stream infections in pediatric ICU patients (Pfaller, 2007). The present study particularly focuses on neonatal and pediatric population because multiple risk factors associated with candidemia are commonly found in this age group. The study also throws light on the fact whether candidemia is more common in the age group of 0 to 12 months of age or in 1 year to 18 years of age group. Thus a combined effect of presence of risk factors associated with exposure to the pathogen is associated with occurrence of infection in this age group. The study estimates the prevalence of neonatal and pediatric patients of candidemia.

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Another important aspect of this study is to look for emergence of candidemia caused by non-*albicans Candida* species (Pfaller, 2007). Studies carried out in India, have reported prevalence of candidemia ranging from 0.16% to 8.1% (Verma, 2003 and Goel, 2009). Cleveland *et al* (Cleveland, 2012) found that infants aged less than 1 year had highest rate of candidemia as compared to 1 year to 19 years of age group. Indian studies have reported the different risk factors such as intravascular catheters, prematurity, low birth weight associated with candidemia (Gupta, 2001; Chowta, 2007). Worldwide *Candida albicans* was the most common species of *Candida* isolated from BSI (Yamamura, 1999). In spite of this, in the past few years, isolation of non-*albicans Candida* species from blood cultures has increased (Cleveland, 2012). In India, non-*albicans Candida* is now the most common cause of nosocomial candidemia (Verma, 2003).

MATERIALS AND METHODS

A cross-sectional prospective type of study was carried out in pediatric patients admitted to the P.I.C.U in a tertiary care hospital. A total of 485 blood samples from clinically suspected cases of blood stream infections of pediatric age group were included in the present study. Candidemia was

diagnosed by isolation of *Candida* spp. from at least one positive blood culture containing pure growth of *Candida* species with supportive clinical features (SrinivasRao, 2014). The study included patients admitted to the P. I. C. U. over a period of 6 months. Patients of the adult age group and patients of the pediatric age group with confirmed diagnosis of any known blood stream infection other than candidemia were excluded from the study. From these cases, 0.5 – 2 ml of venous blood for infants and 2-5 ml venous blood for children was collected before starting antibiotics. Collected blood was transferred into Brain Heart Infusion broth. Brain heart infusion broth was incubated at 37<sup>o</sup> C in aerobic atmosphere. After incubation at 37<sup>o</sup>C, they were sub-cultured thrice (1<sup>st</sup>, 3<sup>rd</sup>, 7<sup>th</sup>) day of incubation) on Sabouraud Dextrose Agar (SDA) with chloramphenicol in duplicate. One SDA was incubated at 37<sup>o</sup>C and other at 25<sup>o</sup>C. Both SDA were checked daily for growth till one week. If no growth was observed after one week of incubation in any of the inoculated SDA, negative result was reported. If any pure growth on SDA with characteristic cream color, smooth, pasty colony was observed; Gram stained smear was prepared from colony. If presence of yeast cells with budding was observed in the Gram stained smear, then the growth on SDA was further processed for identification of *Candida* species as *Candida albicans* or non-*albicans* *Candida* by conventional techniques of Germ tube test and Growth on CHROM Agar.

## RESULTS

Out of 485 cases of the clinically suspected cases of blood stream infections, 313 (64.54%) belonged to the age group of 0 to 12 months.

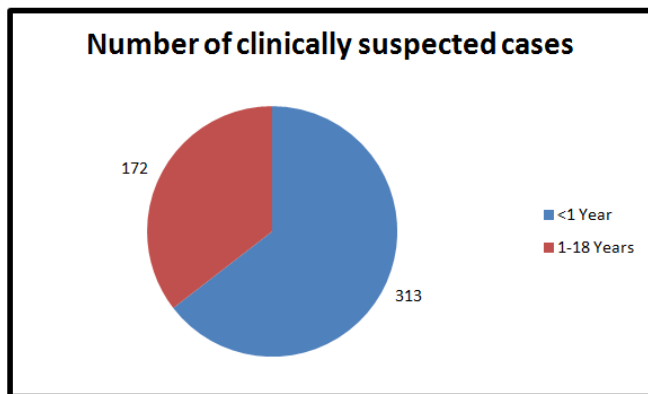


Figure 1. Age wise distribution of clinically suspected cases of candidemia (N=485)

The remaining 172 (34.46%) belonged to the age group of 1 to 18 years. In present study, from 485 clinically suspected cases of candidemia; a total of 5 (1.03%) isolates of *Candida* species were isolated from the blood samples. The difference between the incidences of the confirmed cases in the two age groups was statistically significant (Chi-square test: Goodness of Fit - 'p' value = 0.025). All the confirmed cases of candidemia were observed in neonates. Not a single case of candidemia was found in age group of more than 1 year to 18 years. Presence of intravascular catheter is the most common risk factor associated with all (100%) the cases of candidemia. The second most common risk factor was low birth weight in 4 out of 5 cases (80%). The most common presenting symptom was fever and pallor in 3 out of 5 patients (60%).

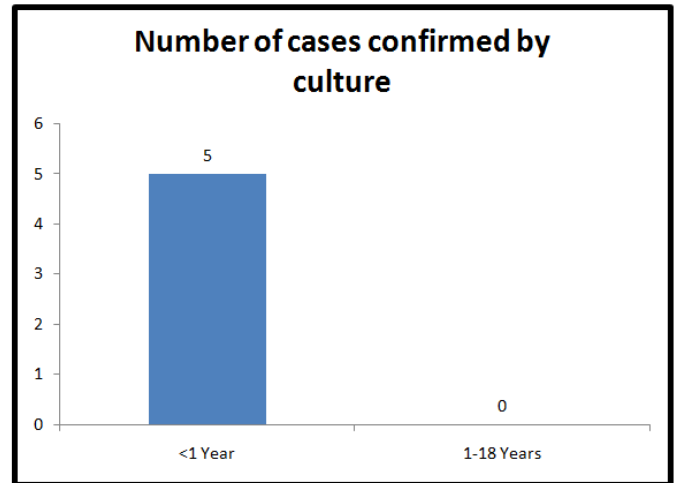


Figure 2. Age wise distribution of confirmed cases of candidemia (N=5)

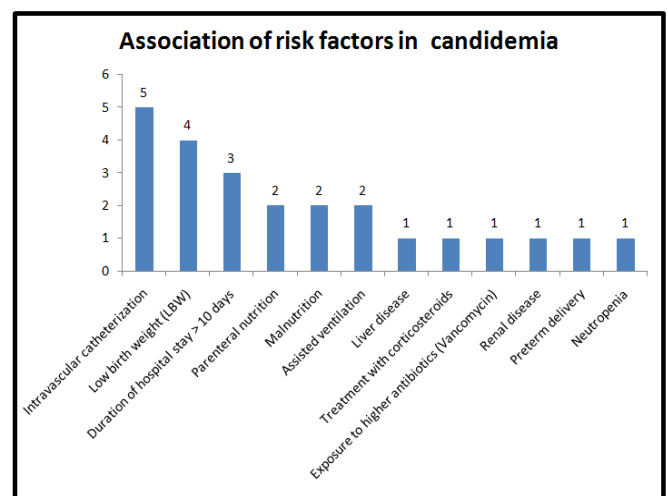


Figure 3. Risk factors associated with candidemia (N=5)

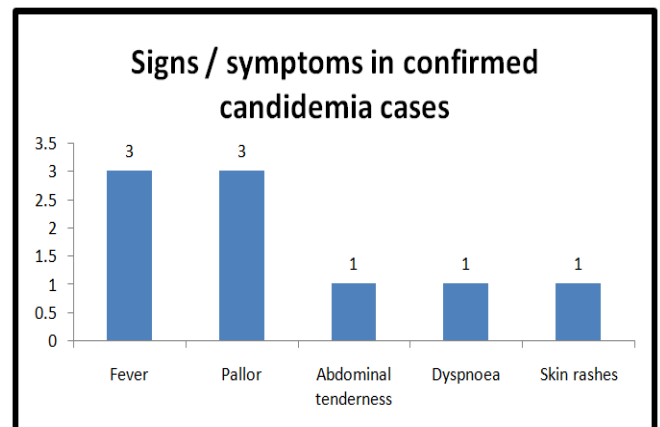


Figure 4. Signs and symptoms of confirmed neonatal candidemia cases (N=5)

Two cases presented with convulsions as a co-morbid condition. One case out of the five cases of candidemia presented as Lower Respiratory Tract Infection and diarrhoea and dehydration respectively. Four (80%) cases of candidemia belonged to non-*albicans*, whereas only one case of candidemia was caused by *Candida albicans*.

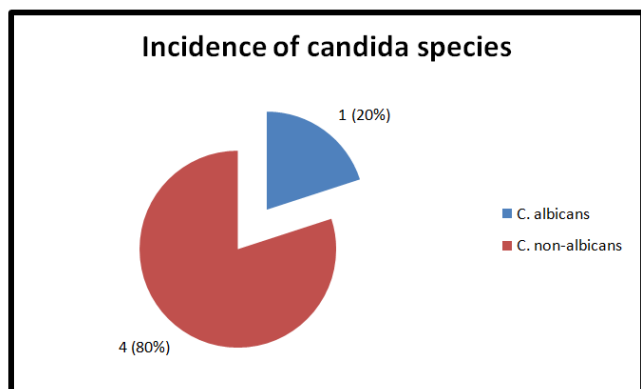
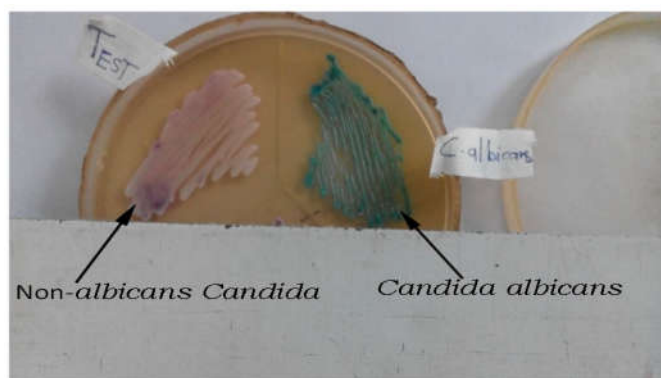


Figure 5. Distribution of Candida species into albicans and non-albicans (N=5)



Photograph shows colony characteristics of non-albicans *Candida* on CHROM Agar (left) and *Candida albicans* on the right shows characteristic green colonies.

## DISCUSSION

In the present study, prevalence of candidemia in clinically suspected cases of Blood stream infections was 1.03%. Other studies carried out in India, have reported prevalence that ranges from 0.16% to 8.1% (Verma, 2003 and Goel, 2009). One of the possible important factors for the difference reported in the present study and previously conducted studies may be, geographical variation as prevalence of candidemia will vary from one geographical region to other due to environmental conditions, awareness about proper hygiene, lack of aseptic precautions during the procedure of intravascular catheterization, wanton use of broad spectrum antimicrobial agents and limited sample size of the present study. The study concluded that infants aged less 0 to 12 months had higher prevalence of candidemia as compared to the age group of 1 to 18 years.

This difference in prevalence of candidemia in different age group was found to be statistically significant. These findings of greater prevalence in 0 to 12 months age group as compared to 1 to 18 years age group resounded with the findings stated in a population based laboratory surveillance study conducted by Cleveland *et al.* (2012). Possible reasons for this may be colonization by *Candida* species in neonates during their passage through the vagina, presence of other predisposing factors like low birth weight, prematurity that have a more significant impact on neonates compared to children of age group 1 year to 18 years (Cleveland, 2012). The present study found that the most common risk factor that was associated with all (100%) confirmed cases of candidemia were

indwelling intravascular catheters. Indwelling intravascular catheters were reported as an important risk factor for candidemia by other studies (Cleveland, 2012 and Gupta, 2001). The second most prevalent risk factor associated with candidemia according to the present study was found to be Low Birth Weight in four (80%) cases. These results are in line with the reports of other Indian studies (Goel, 2009 and Gupta, 2001). Surprisingly, a HIV positive status as a significant risk factor reported by Chowta *et al.* (Chowta, 2007), was not found in the present study as none of the positive cases reported a positive HIV status. The importance attributed to premature birth as a significant risk factor for candidemia by Gupta *et al.* (2001), was significantly reiterated by the present study as one positive case reported preterm delivery.

The present study reported greater number (80%) of candidemia infections caused by non-albicans *Candida*, compared to those caused by *Candida albicans* (20%). These findings are comparable with other studies (Chowta, 2007; Verma, 2003; Kothari, 2008). The probable reason for this shift from *Candida albicans* to non-albicans *Candida* infection may be due to increased use of antifungal triazoles like fluconazole, to which isolates of non-albicans *Candida* species show resistance (Cleveland, 2012). This along with improved ability to colonize the skin and grow in parenteral nutrient solutions may contribute to the dominance of non-albicans species (Levy, 1998). This institution based study had several limitations like small sample size, shorter duration of study and final outcome of the patients was not looked for. These factors could well underestimate the results obtained. Thus the study not only determined the prevalence of candidemia in our geographical area but also relates candidemia to its significant risk factors in neonates.

## Conclusion

As candidemia is treatable with effective use of antifungal drugs its early diagnosis should be made possible. The study estimated the prevalence of candidemia and its associated significant risk factors. These risk factors can be eliminated or limited to prevent occurrence of candidemia. Confirmed diagnosis of candidemia in patients with blood stream infections of pediatric age group is helpful for proper management with antifungal agents. Isolation and correct identification of *Candida spp* will be helpful for in vitro antifungal susceptibility test. Further studies taking into account factors like large sample size, rapid confirmatory diagnostic techniques like Bactec blood culture will improve rate of isolation of *Candida* species from patients of candidemia. Additional studies can be carried out to identify *Candida* up to species level.

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