

Blood stream infections with *Candida* species: a prospective study in a tertiary care center

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Abstract

Aims and Objectives: To study the profile of blood stream infections with *Candida* species, their current epidemiological trend at our setting, clinical management, resistance trends and outcome in terms of mortality. **Methods:** This is a prospective observational study conducted among all adult in-patients, at AIMS, Kochi from August 1st 2014 to February 28th 2016, both in wards and ICUs, who have positive isolates of *Candida* species in bloodstream infection among the positive blood culture samples. Incidence rate of Candidemia was calculated and distribution of Candidemia with respect to characteristics like age, gender, comorbid illness, mechanical ventilation, prior antibiotic therapy, prolonged ICU stay. **Results:** Out of 1600 blood stream infection isolates, Candidemia was fourth most common blood stream isolate infection in our study with an incidence rate of 7.5%. *Candida tropicalis* was the predominant species in our study (30.8%). Mortality rate due to Candidemia was (61%). Urethral catheterization, Central venous access, neutropenia at presentation, prior antibiotic therapy, renal failure, Dialysis patients, prolonged ICU stay were some of the risk factors found to be statistically significant in assessing the mortality of patients in our study with a p value of <0.001. **Conclusion:** All patients with Candidemia should be treated with an antifungal agent at the earliest without any delay, as delay causes increase in mortality. All vascular catheters should be removed to help clear *Candida* from blood more quickly. Improved survival was found with the use of an Echinocandin and the removal of central venous catheters.

Keywords: *Candida*, Candidemia

Introduction

Candidemia describes the presence of *Candida* species in the blood [1,2]. Invasive Candidiasis embodies a variety of diseases including Candidemia, disseminated Candidiasis, meningitis, and endo-phthalmitis. Most common form of invasive Candidiasis is Candidemia. Candidemia is a life-threatening affliction in most of the patients. Invasive Candidiasis has been of a concern as there is increased length and cost of hospitalizations as well as morbidities/ mortalities of patients [1,3,4,5]. Currently Candidemia is the

4th most common etiological agent nosocomial bloodstream infections [6,7]. Certain ICU populations, especially HIV and burn victims, are at even higher risk for *Candida* infection than is the typical ICU patient. Hence, *Candida* in a blood culture should never be viewed as a contaminant and should always prompt a search for the source of the bloodstream infection.

In the last 2 decades a change in the epidemiology of Candidemia has been noticed across the world [8,9,10,11,12]. With the change in the spectrum of *Candida* species causing Candidemia incidence of antifungal resistance of those yeasts are also on

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rise. With a high mortality rate of 35–75% early antifungal treatment is essential for survival [13,14,15].

Objectives of Our Study- The primary objective: Incidence of bloodstream infections with *Candida* species among the total number of positive bloodstream infections in a tertiary care hospital in Kerala over a period of 1.5 year. Secondary objective is to study distribution of Candidemia with respect to characteristics like age, gender, comorbid illness, mechanical ventilation, prior antibiotic therapy, prolonged ICU stay, indwelling device, to study current pattern of antifungal susceptibility and to determine the outcome, in terms of ICU admission and mortality.

Materials and Methods

All adult in-patients admitted to Amrita Institute of Medical Sciences, Kochi, above 18 years of age, who have positive isolates of *Candida* in bloodstream infections among the positive blood culture samples received to the Microbiology department from August 1st 2014 to February 28th 2016, have been included in this study after getting written informed consent. A total of 1600 patient were included in this study.

Patients referred from another healthcare facility, having positive blood isolates of *Candida* and have been reconfirmed with Candidemia isolate on repeat blood sample test in Amrita Hospital will be included in the study population.

Patients in Medical ward as well as Medical ICU will be included in the study, provided they satisfy the other inclusion criteria.

Results

Table-1: Frequency of Candida Species.

Species	Frequency	Percentage
<i>Candida Albicans</i>	27	22.5%
<i>Candida haemolunii</i>	21	17.5%
<i>Candida parapsilosis</i>	27	22.5%
<i>Candida tropicalis</i>	37	30.8%
*Other Non <i>Candida Albicans</i>	8	6.7%
Total	120	100%

**Other Non-Candida Albicans Include: C.Famata, C.Glabrata, C.Guilliermondii, C.Rugosa And C.Krusei*
Results of the study are recorded in the tables as listed here

Inclusion criteria- Adult in-patients (age>18 years) from August 1st 2014 to February 28th 2016, who have positive isolates of *Candida* in bloodstream. Patients referred from another healthcare facility, having positive blood isolates of *Candida* and have been reconfirmed with Candidemia isolate on repeat blood sample test. Patients in Medical ward as well as Medical ICU

Exclusion criteria- Patients with non-Candidemia yeast in blood isolate are excluded from the study.

Sample size- Based on the incidence rate of Blood stream infections with *Candida* among Adults, reported in an earlier publication(Bassetti M, Merelli M, Righi E et al) [3] and with 95% of confidence and 20% allowable error, minimum sample size comes to 1600 samples of any infection among adults.

Ethics and Consent- Written informed consent was obtained from the study subjects participating in the study. There were no ethical or social dilemmas associated with this study and approval was taken from ethical committee before beginning the study.

Statistical Methods- Percentage incidence rate of incidence of blood stream infections with *Candida* among the total number of positive blood stream infections will be computed. To test the statistical significance of the association of various distributive factors of blood stream infections, chi square test will be applied. To obtain the association between outcome and selected variables, chi-square test and continuity correction method were applied. P value of < 0.05 was considered significant.

Table -1: Frequency of Candida Species

Table -2: Mortality Rate Due To Candidemia in Patients Who Were Treated With Different Antifungal

Table-3: Survival Rate in Candidemia Patients With Relation To ICU Stay

Table -4 Multivariate Analysis for Significance

Analysis of the observations are presented in the following figures

Figure -1 Survival Rate in Patients with Candidemia

Figure-2 Mortality Rate Due To Candidemia According To Species Distribution

Table-2: Showing Mortality Rate Due To Candidemia in Patients Who Were Treated With Different Antifungal.

Treatment Given	Outcome				p Value
	Death		Alive		
	n	%	n	%	
Amphotericin [14]	5	35.7%	9	64.3%	0.115
Caspofungin [11]	9	81.8%	2	18.2%	
Fluconazole [77]	48	62.3%	29	37.7%	
Micafungin [7]	3	42.9%	4	57.1%	
Voriconazole [11]	8	72.7%	3	27.3%	

Table-3: Showing Survival Rate in Candidemia Patients With Relation To ICU Stay.

	Duration of ICU Stay	Succumbed	Survived	Total	P Value
ICU Stay	<= 7 Days	22(39.3%)	34(60.7%)	56(100%)	<0.001
	>7 Days	51(79.7%)	13(20.3%)	64(100%)	
	Total	73(60.8%)	47(39.2%)	120(100%)	

Table-4: Multivariate Analysis.

Duration of ICU stay	Significance	Odds Ratio	95% C.I For O.R	
			Lower	Upper
Urethral catheterisation	0.001	22.078	3.804	128.125
Mechanical ventilator	0.042	4.305	1.056	17.544
ICU Stay	0.000	15.509	3.817	63.006

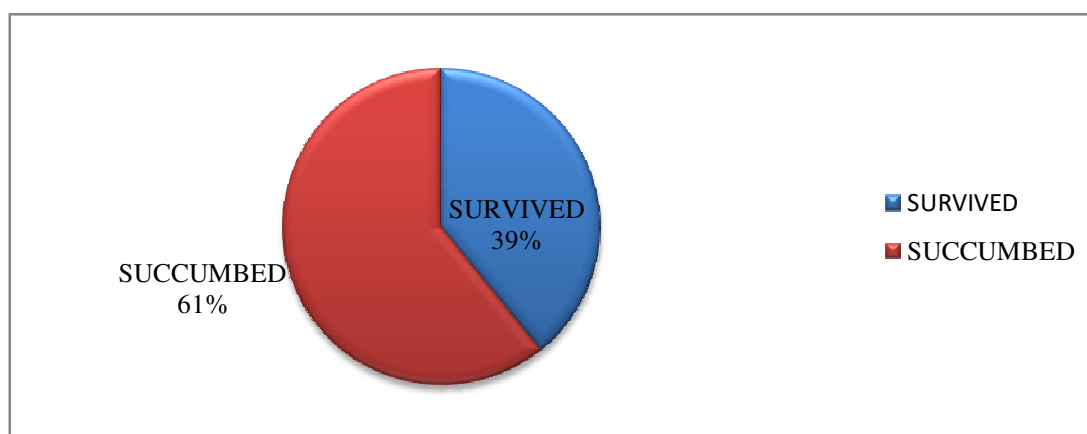


Figure-1: Survival Rate in Patients with Candidemia

Mortality rate due to candidemia according to species wise distribution*Other Non Candida Albicans include: *C.famata*, *C.glabrata*, *C.guilliermondii*, *C.rugosa* and *C.Krusei*

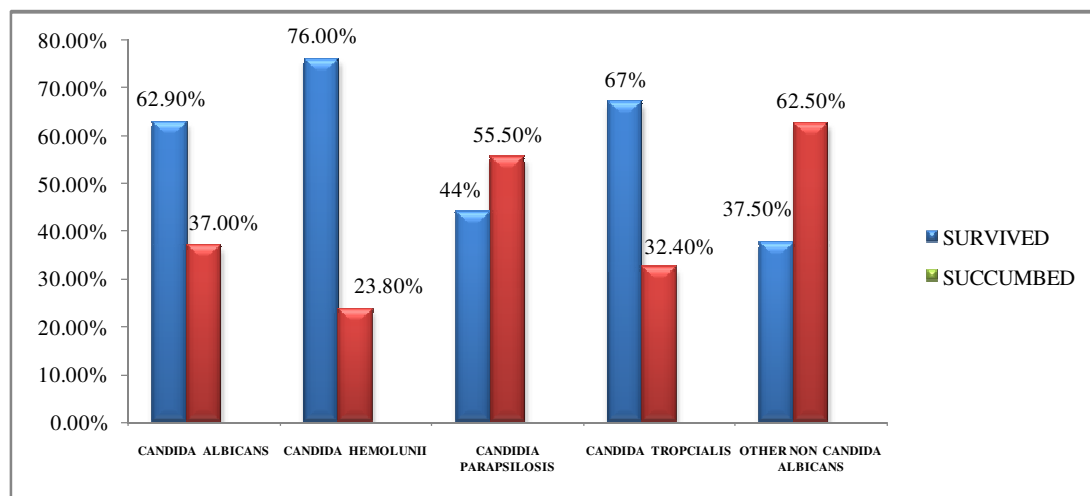


Figure-2: Mortality Rate Due To Candidemia According To Species Distribution

Discussion

We found an overall incidence of 120 cases of Candidemia among 1600 positive blood cultures over 1.5 year with an incidence of 7.5%. Candidemia was fourth most common blood stream isolate infection in our study after Klebsiella pneumonia, Escherichia coli and Staphylococcus aureus. In another prospective, nationwide, multicenter, observational study was conducted at 27 Indian ICUs from April 2011 to September 2012 in India, 1400 Candidemia cases were isolated. A study done in SGPGI Lucknow in 2002 found to have 1.61% incidence of blood stream infections due to Candidemia and it was 8th most common blood stream infection. In Gangaram hospital, the incidence was 1.74%, while in Rohatk medical college it was 8.1%, 6% in AIIMS, and 6.9% in MAMC New Delhi. Most of the people with Candidemia in our study were >60 years old (39.2%), which was in concordance with other studies where most of the Candidemia isolates belonged to patients with mean age group between 59.0–66.2 years [16,17].

Most of the patients with Candidemia in our study were Males (60.8%). Patients with Candida non albicans (93) were more compared to Candida albicans (27) in our study. Candida tropicalis (30.8%) was the predominant species in our study. This is in contrast to the developed world, where *C. tropicalis* uniformly less common (5.6–12.0%) [3-7], and *C. albicans* (45.0–74.0%) and *C. glabrata* (16.7–22.6%) are more prevalent

[18,19,20] where as we have encountered *C. glabrata* Candidemia in only 0.83% of patients. In an earlier study at the coordinating centre, 82% of health care providers were found to carry yeast on their hands and 80% were *C. tropicalis* [11]. Therefore, horizontal transmission and compromise of infection control systems are distinct possibilities for the high rate of *C. tropicalis* candidemia in India. The high rate of *C. tropicalis* candidemia was observed in other Asian countries as well [21]. Proper hygienic measures are required to curb the incidence of horizontal spread of Candidemia. Most of the Cases of Candidemia were admitted under General Medicine department (30%). Co-morbidities of our patients are similar to a certain extent to earlier reports. In the current study frequency of Candidemia was higher in Diabetic population (63.3%). Earlier studies have showed that they have also reported sizable proportions of diabetes (10.7–28.0%) in their Candidemia population [1-3, 6,9,10,13,14]. 5% of our patients with Candidemia had an underlying hematological malignancy, which was less compared to other studies where the incidence was 24.6–36.1% [2,14].

Patients with Candidemia who had HIV infection in our study were only 1.7%, which was almost in concordance with other studies, where the frequency was 4.0–6.0%. [22,23,24,25]. About 9.2% of the patients with Candidemia in our study were neutropenic at presentation, which was almost

similar to other studies where the frequency was 6.6–19.7% [4, 6, 26,27,28,29]. Only 1.7% of the patients in our study with Candidemia had a prior abdominal surgery, which was less compared to 44.7–66.1% seen in other series of studies[1,2]. Among types of surgery, abdominal surgery is considered a leading risk factor for Candidemia [15]. Central venous catheterization was present in 66.7% of the patients with Candidemia in our study which was almost in concordance with other studies where the incidence was found to be 88.5–100% in other studies [1,14]. Invasive mechanical ventilator was present in 49.2% of the patients with Candidemia in our study as compared to 72.1–97.4% in other studies [1,14]. Urinary catheterization was present in 73.3% of the patients with Candidemia in our study compared to 86.7–97.4% in other studies [1,10], which was almost in concordance with our study.

Frequency of Candidemia in patients who were on Hemodialysis was 19.22% compared to 17.5–32.5% [3,9] in other studies, which was in concordance with our study. Frequency of Candidemia in patients who were on TPN was 15% which was less compared to 43.7–71.1% in other studies [1,3]. Candidemia was present in 36.7% of patients in our study who received prior antibiotic therapy, 31.7% of patients who had prior renal failure, 6.7% of patients who received prior corticosteroid therapy, 1.7% of patients who received solid organ transplant therapy. 73 people among 120 people in our study (60.8%) with Candidemia succumbed to their illness which is higher compared to the EPIC II international series where they found a mortality of 42.6% [14]. Mortality rates vary across the globe, they vary between 35–75% [1]. Candidemia-attributable mortality also varies widely (5.0–49.0%) between centers [1,2,5,16].

Urethral catheterization, Central venous access, Mechanically ventilation, Neutropenia at presentation, prior antibiotic therapy, renal failure, Dialysis patients, on TPN, prolonged ICU stay were some of the risk factors which were found to be statistically significant in our study while assessing the mortality of patients in our study with a p value of <0.001. In our study 3 variables were found to be significant while assessing the outcome in terms of mortality, they are Urethral catheterization, Mechanical ventilator and ICU

stay. If patients were urethrally catheterized, there was 22 times more chance of succumbing to their illness due to Candidemia than if they were not urethrally catheterized. If patients were on mechanical ventilator, there was 4 times more chance of succumbing to their illness due to Candidemia than if they were not mechanically ventilated. If patients had prolonged ICU stay, then there were 15 times more chance of succumbing to their illness due to Candidemia than if they did not have any ICU stay.

Conclusion

We conclude with an inference that all patients with Candidemia should be treated with an antifungal agent at the earliest, including patients who have only one blood culture that yields Candida and those with a vascular catheter tip that yields Candida. Any delay in initiation of treatment, showed an increase in mortality rates. All vascular catheters should be removed because removal has been shown to help clear Candida from blood more quickly. Repeated blood cultures should be obtained to ascertain that the fungemia has resolved, and treatment should continue for 2 weeks after the date of the first negative blood culture. Improved survival and clinical success was found with the use of an echinocandin and the removal of central venous catheters.

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