



To Study The Magnitude of Candidemia in Intensive Care Unit Patients in S.M.S. Medical College and Hospitals, Jaipur

KEYWORDS

Intensive care unit (ICU), Candidemia, Non-albicans Candida species, Antifungal susceptibility.

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ABSTRACT *Background: The incidence and prevalence of candidemia is on a rise worldwide. Non-albicans Candida species has emerged as major cause of candidemia globally. Incidence of antifungal resistance is rising to especially in ICU.*

Objectives: To study the magnitude of candidemia in ICU antifungal susceptibility pattern and various risk factors associated with candidemia.

Materials and Methods: All Candida isolates from blood stream infection of ICU Patients (555) were included in the study period (April 2015-June 2015). The isolates were identified with automated Vitek-2 compact system of Biomatrix, Germany, using the YST ID cards and their antifungal susceptibility was performed using AST YS 06 Cards.

Results: A total of 24 (4.32%) Candida isolates were found among 555 ICU patients Candida tropicalis (33.33%) was the most common isolate followed by Candida krusei, Candida albicans, Candida parapsilosis, Candida pelliculosa, Candida pseudotropicalis and Candida guilliermondii. Among the 24 Candida isolates, resistance to the fluconazole was 37.5%, to voriconazole 0%, to amphitericin B 12.5%, flucytocin 25%, caspofungin 8.33% and micafungin 8.33%. The risk factors commonly associated with candidemia patients were long term antibiotic therapy (54.17%), central venous catheters (37.15%), urinary catheters (16.67%), ventilator (16.67%) and low birth weight (16.67%).

Conclusion: Candidemia is emerging as a significant problem in hospitalized patients, especially in ICU setups. Non-albicans Candida species are the major cause of candidemia as found in our study.

INTRODUCTION

Candida species are the most common cause of fungal infections worldwide. They may manifest as a simple cutaneous or mucocutaneous infections to more severe systemic infections. Presence of *Candida* in the blood stream is termed as Candidemia. Increased incidence of candidemia is seen in hospitalized patients especially admitted in intensive care units (ICUs). It is reported as the 4th common cause of blood stream infection (BSI) in USA, with a mortality rate as high as 30-40%.¹ It also leads to prolonged hospital stay and increase economic burden on the patients. Several predisposing factors are responsible for the occurrence of candidemia in ICUs. These include prolonged use of broad spectrum antibiotics, central venous catheter (CVC), prematurity, low birth weight (LBW), total parental nutrition (TPN), urinary catheter, and mechanical ventilation.² Recent report also suggest a shift in distribution of candida species from candida albicans to non albicans candida in cases of candidemia.³ Increased incidence of antifungal drug resistance has become a major cause of concern in management of candidemia.⁴ Therefore species identification and determination of antifungal susceptibility pattern of the candida isolates will help in early diagnosis and prompt therapeutic intervention.

The present study was aimed at determining the magnitude of candidemia, its species distribution and antifungal susceptibility pattern in patients admitted in various ICUs of our hospital, a tertiary care centre in North India.

Materials and Methods

This study was carried out in the department of Microbiology, S.M.S Medical College, Jaipur, a tertiary care center in Rajasthan during the period April 2015 to June 2015. Ethical clearance for the study was obtained from the Institutional Ethics Committee. Blood samples were collected aseptically in brain heart infusion (BHI) broth from suspected cases of BSI in ICUs., with completely filled prescribed proforma and informed consent. The BHI bottle was incubated at 37°C in the laboratory and observed daily for visible growth. Subculture was performed after 48 hours and on 7th day before being reported negative. If visible growth was observed earlier, they were sub cultured on primary inoculation media i.e. Blood agar, Mac Conkey agar. Colonies of Yeast on blood agar were identified by their smooth creamy colored appearance and Gram's staining. All isolates of *Candida* were characterized and subjected to antifungal susceptibility testing using the Vitek-2 YST ID and AST YS 06 cards as per to manufacturers' (Biomatrix) instructions and results were evaluated.⁵

Statistical analysis

Descriptive statistics were analyzed using 2 tests. A two-tailed P-value <0.05 was considered statistically significant.

Result

A total of 555 patients admitted and suspected of BSI were included in the study period from April 15 to June 15. 132 (23.78%) samples were culture positive out of which 108 (19.46%) were aerobic bacterial pathogens and 24 (4.32%) were *Candida* species, these confirming candidemia in them.

Male preponderance was seen with male to female ratio 1.4:1. Maximum incidence was seen in neonatal age group (33.33%) followed by old age group (>55yrs) 29%.

Table 1
Various predisposing factors for candidemia

Predisposing factors	Total case	%
Prematurity	1	4.17
Low birth weight (LBW)	4	16.67
Diabetes mellitus	3	12.5
Post operative condition	2	8.33
Carcinoma and Chemotherapy	1	4.17
Ventilator	4	16.67
Central line/CVC	9	37.15
Urinary catheter	4	16.67
Prolong antibiotic	13	54.17
Parental nutrition	2	8.33%

Majority of cases had more than one predisposing conditions, commonest one were long term antibiotic therapy (54.17%) and presence of central venous catheter (37.15%). 66% of patients had multiple predisposing factors association for candidemia.

Table:2
Distribution of candida albicans and non albicans

Species	No.	Percent
Candida albicans	4	16.67%
non albicans candida	20	83.33%
Total	24	100

Out of 24 candida isolates only 4 (16.67%) were of *Candida albicans* and the rest 20 (83.33%) were of *non albicans candida*.

Table:3
Distribution of Candida according to species by Vitek-2 yeast identification

Species	Total no.	Percent
Candida tropicalis	8	33.33%
Candida krusei	6	25%
Candida albicans	4	16.67%
Candida parapsilosis	2	8.33%
Candida pelliculosa	2	8.33%
Candida pseudotropicalis	1	4.17%
Candida guilliermondii	1	4.17%
Total	24	100

Maximum isolates were of *C.tropicalis* (n=8, 33.33%), followed by *C.krusei* (n=6, 25%), *C.albicans*(n=4,16.67%),*C.parapsilosis*(n=2,8.33%), *C.pelliculosa*(n=2,8.33%), *C.pseudotropicalis* (n=1, 4.17%) and *C. guilliermondii* (n=1. 4.17%).

Table:4
Antifungal Resistance pattern of candida isolates

Species	Resistance (Percentage)					
	Fluconazole	Voriconazole	Amphotericin B	Flucytosine	Caspofungin	Micafungin
<i>C. albicans</i> (4)	50%	0%	25%	25%	25%	0%
<i>C. tropicalis</i> (8)	12.5%	0%	0%	0%	0%	0%
<i>Candida krusei</i> (6)	100%	0%	16.67%	83.33%	16.67%	0%
<i>C.parapsilosis</i> (2)	0%	0%	0%	0%	0%	0%
<i>C.pseudotropicalis</i> (1)	0%	0%	0%	0%	0%	0%
<i>C. guilliermondii</i> (1)	0%	0%	0%	0%	0%	0%
<i>C. pelliculosa</i> (2)	0%	0%	0%	0%	0%	0%
Total(24)	37.5%	0%	12.5%	25%	8.33%	0%

Fluconazole shows maximum resistance to candida species where as voriconazole and micafungin had least.

Discussion

Candidemia is becoming a common occurrence in patients admitted in ICUs. Intense therapy, invasive procedures, various underlying diseases leads to BSI leading to sepsis with various bacterial and fungal agents. Therefore isolation, identification and antimicrobial spectrum is essential for management of sepsis. In the present study we identify the magnitude of candidemia from the blood culture sample received from patients admitted in various ICUs of a tertiary care hospital and characterized the candida isolates up to species level. Since various species differ in their antifungal susceptibility pattern, we also tested.

The incidence of candidemia in our study was 4.32% which correlate well with studies of Verma A K et al⁶ and Kumar C P et al⁷ who reported candidemia in 3.89% and 5.7% cases of blood stream infection in ICUs respectively.

In our study candida ranks as the 4th common isolates from blood samples of ICUs patients, Wisplinghoff et al⁸ from USA also reported candida at 4th rank. In reports from other areas, Giri S et al⁹ from Tamilnadu reported it as the 6th common isolates where as Verma A K⁶ et al from SGPGL, Lucknow reported it as 8th common isolates. This shows that incidence of candidemia in ICUs are increasing steadily and variation in frequency may be due to differences in management modalities, existing infection control practices and variable host factors. In ICUs incidence of candidemia or blood stream infection depends on various factors like long term antibiotic therapy, presence of central venous catheter, low birth weight, mechanical ventilation.

Our study shows that neonates and older age group patients of >55yrs were more prone to developing candidemia which also reported by Jorge A Guzman et al¹⁰ (<7 days and >61 yrs), Chun-fang Ma et al¹¹ (>65 yrs)

which shows that immunity is lower at early and extreme of age where in high risk area like ICUs.

Male to female ratio is 1.4 :1 in our study which shows that there is no significant gender preponderance in development of candidemia.

Our study shows prolonged antibiotic as a significant risk factor for development of candidemia in ICUs patients (54.17%), as has also reported by S Giri et al⁹ 64% and Xess et al¹² 71.2%. Our study also shows that patients with central venous catheter 37.15% were at significant risk of developing candidemia as also shown by studies of Chung fung Ma et al¹¹ 46% and S Giri et al⁹ 56%. Similarly other risk factor for candidemia in our study were urinary catheterization 16.67%, mechanical ventilation 16.67%, Low birth weight 16.67%, Diabetes mellitus 12.5%, post operative condition 8.33%, total parental nutrition 8.33%, pre term babies 4.17%, cancer and chemotherapy 4.17%. There were 66% of patients had more than one predisposing conditions among these. Many other studies have reported similar results.

Prevalence of candida species in blood stream infection has increased worldwide in the last decades. In the last few years occurrence of non albicans candida species are steadily increasing. In the present study non albicans candida accounted for 83.33% which also correlate with study of Jaswinder K Oberoi et al¹³ 83.2% and M Bhatt et al¹⁴ 85.3%.

In our study *C.tropicalis* was the predominant isolates 33.33%, similarly Shiv prakash et al¹⁵ and Verma A K et al⁶ reported *C.tropicalis* as the most common cause of candidemia at 35.6% and 33% respectively.

In present study all the 24 isolates (100%) were sensitive to voriconazole. Kumar et al⁷, and Xess et al¹² reported similar results with voriconazole

Although fluconazole still remain a safe and effective choice for the treatment of candidemia, are increasing trends of fluconazole resistance has been reported in many studies as 37.5% by Gupta et al¹⁶, 36% by Kothari et al¹⁷, 25% by Adhikari et al¹⁸ and 11.7% by Xess et al¹². In the present studies 37.5% of candida were resistance to fluconazole. *Candida krusei* having intrinsically resistance to fluconazole reported. The changing spectrum of candida species causing candidemia from *C.albicans* to Non albicans candida esp. *C.glabrata* and *C.krusei* is responsible for fluconazole resistance.

In present study resistance to Amp B among all candida isolates was 12.5%. Similar results were reported by Jaswinder K Oberoi et al¹³ 10.4% and M Bhatt et al¹⁴ 8%. Although Amp B has a rapid cidal action against most strains of candida species (esp. *C.albicans*), it is not the first choice due to associated nephrotoxicity and the newer lipid formulation having a better cidal effect profile. However in the developing country like India, fluconazole is the most widely drug of choice for treatment of candidemia due to its low cost, higher bioavailability along with intravenous (IV) formulation.

Resistance to 5FC among the 24 candida isolates was seen in 25% isolates in the present study. In other studies a variable range of resistance to 5FC was reported, 37% by M Bhatt et al¹⁴, 11.46% by Vinodkumar et al¹⁹, where as N Pahawa et al²⁰ reported 0% resistance in their studies.

Primary resistance to various mechanisms is responsible for resistance to 5FC among candida species.

In present study 8.33% isolates were resistant to caspofungin which correlated with the study of D Farmakiotis, J J Tarrand et al²¹ 10.3% from USA. In other study by Michael A. Pfaller et al²² and Maria Teresa Montagna et al²³ found 1.9% and 3.8% resistance respectively. Jaswinder K O et al¹³ reported 100% sensitivity to caspofungin in his study.

In our study all isolates were sensitive to micafungin similar result were found in the study of D. Farmakiotis, J.J. Tarrand et al²¹ in USA.. However Michael A. Pfaller et al²² from USA and Maria Teresa Montagna et al²³ from Italy reported 1.9% and 1.5% resistance to micafungin respectively in their study.

Echinocandin resistance in susceptible species is always acquired during therapy, should undergo susceptibility testing and be treated with an alternative antifungal agent if possible.²⁴

Conclusion

This study therefore emphasizes the need for a continuous surveillance of Candidemia in the patients admitted to intensive care units of the hospital. Candida species identification up to species level and determination of their antifungal resistance pattern will help the clinician in the management of candidemia and reduce the morbidity and mortality in these patients.

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