Epidemiological profile of candida isolated from septicemic patients

Thressia Thomas[1], Meena Dias[2,*]

[1]Post Graduate Resident, [2]Associate Professor, Dept. of Microbiology, Fr Muller Medical College, Kankanady, Mangalore, Karnataka, India

***Corresponding Author: Meena Dias**
Email: drmeenadias@gmail.com

Received: 24th August, 2018 **Accepted:** 26th November, 2018

Abstract

Introduction: *Candida* is an important cause of blood stream infections (BSI). It ranks fourth in the United States and seventh in Europe. It is a leading cause of morbidity and mortality in critically ill patients. There is an epidemiological shift from a predominance of *Candida albicans* to non *albicans Candida* species in recent decades. Speciation of *Candida* can help in better approach towards outcome of the patients and to know the intrinsic resistance of various *Candida* species to antifungal agents.

Objectives: To determine the epidemiological profile of *Candida* infection in septicemic patients and to identify the *Candida* species isolated.

Materials and Methods: A hospital based descriptive study was conducted over a period of 2 years in a tertiary care centre. *Candida* was isolated in blood culture from 54 patients. Candida isolates were identified to the species level, using both conventional and automated techniques.

Results: The most common *Candida* species isolated were *C.parapsilosis complex, C.tropicalis, C.albicans, C.krusei, C.glabrata, C.haemulonii, C.firmetaria and C.guillermondii var membranifaciens*. Significant risk factors for candidemia includes HIV/AIDS, diabetes, antibiotic therapy, chemotherapy, presence of intravascular catheters, malignancy, surgery, parenteral nutrition. 51.85% of the patients received antifungal therapy with Fluconazole (71.43%) being the most common treatment option which is followed by Voriconazole (10.71%) and Amphotericin B (7.14%).

Conclusion: Candidemia is a significant cause of mortality with *C. parapsilosis* and *C. tropicalis* being the predominant pathogens. This study shows a significant epidemiological shift to higher isolation of non *albicans Candida* species.

Keywords: *Candida* species, Epidemiological profile, Septicemic, Risk factors.

Introduction

Fungi have emerged as major opportunistic pathogens causing human disease. *Candida* accounts for nearly 96% of all opportunistic mycoses and is an important cause of blood stream infections (BSI).[1] Among bloodstream infections, *Candida* ranks fourth in the United States and seventh in Europe.[2] It is a leading cause of morbidity and mortality in critically ill patients, with crude mortality rates ranging from 30 - 81%.[1] *C. albicans* was the predominant species constituting up to two thirds of all cases of invasive candidiasis. However, in recent decades, there is a change in the epidemiology of *Candida* infections, with a progressive shift from a predominance of *Candida albicans* to non *albicans Candida* species (including *C. glabrata, C. tropicalis* and *C. krusei*).[2] Indian studies have reported candidaemia rates of 6-18 per cent and an increase in isolation of non *albicans Candida* species.[2] Risk factors for candidaemia includes human immunodeficiency virus infection/acquired immunodeficiency syndrome (HIV/AIDS), diabetes,[1] antibiotic therapy, chemotherapy, presence of intravascular catheters, malignancy, surgery, parenteral nutrition, intensive care unit stay and prior fungal colonization.[3]

Delay in recognition of *Candida* infections and initiation of appropriate antifungal therapy often leads to significant morbidity and mortality rates particularly among critically ill patients. So, from microbiological aspect, identification of these pathogens can help in better approach towards outcome of the patients and to know the intrinsic resistance of various *Candida* species to antifungal agents.

Hence in this study, an attempt has been made to speciate the various *Candida* isolates from septicemic patients and to identify the epidemiologial profile and risk factors associated with *Candida* septicemia.

Materials and Methods

This hospital based descriptive study was conducted in the Department of Microbiology of a tertiary care teaching hospital from June 2015-2017 after obtaining ethical clearance from Institutional ethical committee. All patients from whom *Candida* species were isolated from blood atleast once and patients with one or more of risk factors that predispose to candidemia were included in the study. Patients with *Candida* species isolated from other sites were excluded from the study.

Automated Bactec blood culture (Becton and Deckinnson) samples were collected from patients under all aseptic precautions and isolates were identified depending on colony morphology on Sabouraud's dextrose agar (SDA), germ tube test, growth on Corn meal agar and CHROM agar medium.[4]

These isolates were confirmed by using automated techniques (BD Phoenix).

Demographic data, risk factors, clinical history including treatment and laboratory investigation were also collected. The data obtained was analyzed by software SPSS version 21.0 Chi-square test and Fisher exact test. A p value less than 0.05 was considered statistically significant.

Results

A total of 54 patients were confirmed to have *Candida* septicemia with male: female ratio being 2:1. Majority of the patients were in the age group of 18-50years (42.6%) with male preponderence. 13 out of 54 patients were children less than 17 years of age (9 infants and 4 children).16.66% (9) of patients were infants between 1 month to 1 year of age.

Table 1 and 2 shows the common risk factors associated with *Candida* septicemia in adults and children. 46.15% of preterm children and 38.4% of term children were delivered by LSCS and 38.46% of term children were delivered by LSCS. Majority of the patients who were critically ill were admitted in ICU (57.4%) than wards (42.49%).

In adults, who were diagnosed with malignancies, the most common were abdominal (37.5%) followed by hematological (31.25%), oral (12.5%), lymphoma (12.5%) and CNS (6.25%). 29.63% of malignancy patients developed neutropenic fever. There was no history of HIV or organ transplantations in of the patients. The most important predisposing factors that contributed to candidemia was abdominal surgeries like explorative laparotomy (50%) followed by wound debridement (11.11%), wide excisions at local site (5.55%) and cranial surgeries (5.55%).

The most common *Candida* species isolated in descending order are *C.tropicalis*, *C.parapsilosis complex*, *C.albicans*, *C.krusei*, *C.glabrata*, *C.haemulonii*, *C.firmetaria* and *C.guillermondii var membranifaciens*. Common *Candida* species isolated from malignancy and surgery patients are included in Table 3.

28/54 (51.85%) of the patients were treated with Fluconazole (71.43%) followed by Voriconazole (10.71%) and Amphotericin B (7.14%). In other patients, antifungal therapy used for *Candida* isolates is shown in Table 4. 36 out of 54 patients were treated successfully. 22.22% of patients expired due to sepsis and associated complications.11.11% of patients were lost for follow up.

Table 1: Common risk factors seen in adults

Risk factors	Adults
Indwelling central line	15
Malignancy	15
Total parenteral nutrition	11
Chemotherapy	11
Abdominal surgery	10
Sepsis	11
Abdominal diseases	6
Malnutrition	3

Table 2: Common risk factors seen in children

Risk factors	Less than 1 month	1 month- 1 year	2-5years	Adolescent age group
Total parenteral nutrition	4	5	1	1
Indwelling central line	3	5	1	2
Low birth weight	3	2	1	1
Preterm	3	1	1	0
Maternal complication	3	3	1	0
Surgery	2	2	1	2

Table 3: Common *Candida* species isolated from malignant (p=0.022) and surgery patients

Candida species	Number	Malignancy		Surgery	
		Present	Absent	Done	Not done
C.tropicalis	15	1	14	5	10
C.parapsilosis complex	14	7	7	3	11
C.albicans	9	5	4	3	6
C.krusei	5	-	5	3	2
C.glabrata	5	1	4	2	3
C.haemulonii	3	2	1	1	2
C.firmetaria	1	-	1	1	-
C.guillermondii var membranifaciens	1	-	1	-	1

Table 4: Antifungal therapy for various *Candida* species

Antifungal	%	*parapsilosis*	*albicans*	*tropicalis*	*haemulonii*	*krusei*	*glabrata*	*firmetaria*	*guillermondi*
Fluco- 20	71.43	9	6	3	1	-	-	1	-
Vori - 3	10.71	1	-	-	-	-	1	-	1
Amph B -2	7.14	-	1	-	-	1	-	-	-
Amp B+ Fluco - 3	10.71	-	-	2	-	1	-	-	-

Antifungal- Antifungal agent; %- percentage;Fluco- Fluconazole; Vori- Voriconazole; Amph B- Amphotericin B

Discussion

Infection with unusual organisms is an increasing problem. Due to advances in medical and surgical management, an increase in nosocomial fungal infection rate has been observed.[5] Candidemia is an emerging problem in healthcare settings. Knowledge of the epidemiology of candidemia can help to salvage patients, who are in the productive age group, with few with underlying medical condition.[1]

In this study, candidemia is most commonly seen in patients between 18-50 years of age (42.6%). Among children, it is most commonly seen in infants less than 1 year of age. On the contrary, other studies[3,6] shows a higher preponderance in extremes of age group.

The common risk factors seen in infants are indwelling central and umbilical catheters, total parenteral nutrition and surgical interventions which is similar to other studies.[7-9] Majority of the infants were low birth weight (LBW) and maternal complications like perinatal depression, oligohydramnios and PROM was noticed. In adults who developed candidemia in our study, the common risk factors were malignancy followed by malnutrition and diabetes mellitus (DM). Malignancy is an important risk factor which is statistically significant (p=0.022). Majority of the patients had abdominal malignancies, followed by hematological and oral. The common hematological malignancy was acute myeloid leukemia (AML) and Non Hodgkins lymphoma (NHL). These patients were malnourished, neutropenic and were on chemotherapy which would have been the contributing factors. Lortholary O et al[10,6] noticed lymphoma (41.8%) and acute leukemia (AL, 33.5%) as common hematological malignancies which is similar to our study. Among solid tumors, they also observed, digestive (45.7%), genital (12.3%), or urinary (8.9%) tract, or the ear, nose, and throat area (11.0%).

In the present study, patients with no malignancy had surgery as one of the risk factors with abdomen being the most common site. Most of the surgeries followed trauma, obstruction, chronic infection or inflammation which is similar to our study.[10]

We did not find any correlation between Central line associated blood stream infection (CLABSI) and *Candida* infection (p=0.523, not significant).All the central venous catheter tips that were pulled out were often but not always, sent to the laboratory. This has resulted in growth in the CVP tips with *Candida* spp. in the absence of a positive blood culture. The standard guidelines for CLABSI was not implemented universally in this study. These constraints have limited the identification of primary CLABSI from non-CLABSI cases.

In patients with candidemia, other bacteria were isolated from various sites like blood, pus, urine and sputum in our study. The most common bacteria are, *Coagulase negative staphylococci* and *Pseudomonas aeruginosa* in blood, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* in pus and *E coli* and *Pseudomonas aeruginosa* in urine. This suggest that *Pseudomonas aeruginosa* is the predominant bacteria isolated from majority of the sample which is similar to a study conducted in AIIMS, New Delhi.[1]

We isolated *Candida tropicalis* as the predominant isolate which is similar to others[1,2,10] and some studies[7] had *Candida parapsilosis complex* as the common pathogen and[9,11] observed *Candida glabrata* as the common pathogen.

Several studies suggest that, time for initiation of treatment may be a more important determinant of outcome than choice of a specific antifungal agent.[12-14] In our study, the most common antifungal therapy used for treatment is Fluconazole followed by Fluconazole - Amphotericin B combination which is similar to Kumar S et al.[17] Majority of the patients with *Candida parapsilosis* infection were treated with Fluconazole. This could be because of increased susceptiblilty to various infections and high exposure to several antibiotics and antifungal agents[16]. On the contrary, another study[18] mentions all candidal isolates to be sensitive to amphotericin B 92% and then fluconazole 36%. *Candida glabrata* is intrinsically resistant to Fluconazole and thus, Amphotericin B is used as the drug of choice. Another study[19] suggest that Amphotericin B is associated with higher mortality in candidemia patients and because of the increased adverse effects like acute renal failure, electrolyte imbalances, gastrointestinal upset etc.

Outcome depends on the immunological status of the patient and use of antifungal agents. Delay in administering systemic antifungal therapy for the treatment of candida bloodstream infection more than12 hours after the first positive blood culture is drawn, is a potential risk factor for mortality.[17,20] Majority of the patients in our study received antifungal therapy after a positive blood culture and responded well to treatment. Survival rate is maximum in the age group of 18-50 years and declines at the extremes of age. This study

shows a higher mortality rate in elderly above 50 years of age which is similar to another study.[3] It could be likely because of co morbidities or reduced immune status of the patient. The mortality is high in patients with *Candida tropicalis* infection and least in *Candida parapsilosis* infection. This is similar to the study conducted by Wang TY et al.[19,17,21,22]

Conclusion

Frequency of candidemia in our population is similar to that reported from other developing countries which suggest that non-albicans species are more common in India and adjacent parts of the world. It is an important cause of mortality with *C. tropicalis and C. parapsilosis complex* being the predominant pathogens. Our study shows a significant epidemiological shift from *albicans* to non-*albicans Candida* species. Thus, early isolation and speciation will aid the clinicians to institute proper antifungal therapy, thereby decreasing the morbidity and mortality. Infection control measures to reduce nosocomial transmission like hand and personal hygiene by healthcare workers, proper catheter care, frequent clinical examination of patients who are weaned off invasive device and antibiotic stewardship must be emphasized.

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How to cite this article: Thomas T, Dias M. Epidemiological profile of candida isolated from septicemic patients. Indian J Microbiol Res. 2018;5(4):508-511.