

**Original Article:****Epidemiology of fungal infections in critical care setting of a tertiary care teaching hospital in North India: a prospective surveillance study**Tirath Singh,<sup>1</sup> Anil Kumar Kashyap,<sup>2</sup> Gautam Ahluwalia,<sup>1</sup> Deepinder Chinna,<sup>3</sup> Sandeep Singh Sidhu,<sup>4</sup>Departments of <sup>1</sup>Medicine, <sup>2</sup>Pulmonary Medicine, <sup>3</sup>Microbiology, <sup>4</sup>Gastroenterology

Dayanand Medical College and Hospital, Ludhiana

**ABSTRACT**

**Background:** During recent years, fungal infections have risen exponentially and are a cause of significant morbidity and mortality in hospitalized patients, especially in the critical care setting. There is paucity of data from India on fungal pathogens.

**Methods:** We prospectively studied patients admitted to medical and surgical critical care section of a tertiary care institute in northern India. The clinical samples of patients were processed in Department of Microbiology for isolation and identification of fungi by using standard protocols over a period of one year. The patients were categorized into fungal infection and colonization groups. The demographic data and risk factors for fungal infection and colonization were evaluated.

**Results:** Ninety one (82.7%) of the 110 patients enrolled in the study, had fungal infection, whereas 19 (17.3%) had fungal colonization. *Candida* were isolated from 85/91 (93.4%) and 19/19 (100%) patients with fungal infection and colonization respectively. There was predominance of non-*albicans Candida* spp both in fungal infection 61/85 (71.7%) patients as well as fungal colonization group 16/19 (84.2%). In non-*albicans Candida* spp., *Candida tropicalis* was the most common isolate observed in both fungal infection (85.3%) and fungal colonization (63.1%) groups. Overall, in patients with fungal infection, candiduria was detected in 68/91 (74.7%) whereas candidaemia was observed in 19/91 (20.8%) patients. The risk factors for fungal infections included urinary catheterization (85.7%), central line insertion (81.3%), mechanical ventilation (52.7%), use of corticosteroids (23.1%), total parenteral nutrition (6.6%) and peritoneal dialysis (3.3%).

**Conclusions:** The emergence of non-*albicans Candida* similar to the trends in the western countries should be a cause of concern in our country. Proper surveillance of fungal pathogens is important to improve quality of care in critical care setting and measures should be focussed to control these infections, especially in patients with these risk factors.

**Key words:** Fungal Infection, Fungal Colonization, Critical Care, Non-*albicans Candida*

Singh T, Kashyap AK, Ahluwalia G, Chinna D, Sidhu SS. Epidemiology of fungal infections in critical care setting of a tertiary care teaching hospital in North India: a prospective surveillance study. *J Clin Sci Res* 2014;3:14-25.

**INTRODUCTION**

The incidence of fungal infections has risen substantially over the past several decades. Extensive and inappropriate use of antimicrobial agents as well as use of immunosuppressant drugs in various diseases has contributed to the increased propensity for opportunistic fungal infections.<sup>1</sup> An important factor for opportunistic fungal infections is

hospitalization of patients, especially in an intensive care unit (ICU). The most common fungi involved in invasive disease in humans are opportunistic yeasts like *Candida albicans* or filamentous fungi like *Aspergillus* spp. Fungi such as *Candida* (except *albicans*), *Fusarium*, *Trichosporon* and *Malassezia* spp., which were previously considered to be non-pathogenic for humans or were only causing human diseases sporadically are now emerging as leading

Received: 5 September, 2013.

**Corresponding author:**

Dr Gautam Ahluwalia, Professor, Department of Medicine, Dayanand Medical College and Hospital, Ludhiana, Punjab, India.

e-mail: dr\_gautam\_ahluwalia@dmch.edu



Online access

[http://svimstpt.ap.nic.in/jcsr/jan-mar14\\_files/oa314.pdf](http://svimstpt.ap.nic.in/jcsr/jan-mar14_files/oa314.pdf)

nosocomial fungal pathogens. These pathogens are associated with increasing morbidity and mortality.<sup>1,2</sup>

Over past two decades, there has been a change in the distribution of *Candida* spp. causing nosocomial infections and emerging species are *C. tropicalis*, *C. glabrata*, *C. parapsilosis*, *C. krusei*, and *C. lusitaniae*.<sup>2</sup> Candidaemia is frequently a life threatening complication in patients admitted in ICUs.<sup>1</sup> The presence of *Candida* species in the urine is also common among hospitalized patients. The principal risk factors include antibiotic therapy, urinary catheterization, surgical procedures, female sex and extended hospitalization.<sup>3</sup> Moreover, multiple site colonization with *Candida* species is also being commonly recognized as a major risk factor for invasive fungal infections in critically ill patients.<sup>4</sup>

There is paucity of data from India on fungal infections in the critical care setting with variable results.<sup>5-11</sup> These studies are mainly from Delhi and there have been sporadic reports from Kolkata, Pune, Chandigarh and Dehradun.<sup>5-11</sup> There is an urgent need for surveillance studies on fungal infections and fungal colonizations from different health care institutions nation-wide to provide data on this subject. It is important to differentiate fungal infection from fungal colonization as colonization may precede fungal infection, especially in the critical care setting.

The present study was done in patients with documented fungal infection or fungal colonization admitted in medical and surgical critical care section of a medical college of North India.

---

## MATERIAL AND METHODS

---

Dayanand Medical College and Hospital (DMCH), Ludhiana, Punjab is a 1000-bed tertiary care institute, providing teaching facilities to undergraduate and postgraduate

students including medical and surgical subspecialties. The institute caters to population from Punjab, Haryana, Rajasthan and Himachal Pradesh. The critical care section has 100 beds. The medical critical care section has medical ICU, pulmonary critical care unit and stroke ICU. The surgical critical care section has surgery ICU and neurosurgery ICU.

A prospective surveillance study was performed in the medical and surgical critical care sections at the DMCH, Ludhiana, from January 1 to December 31, 2009 to identify patients with documented fungal infection or fungal colonization. All adult patients above 18 years of age in whom fungal infection or colonization were clinically suspected and confirmed as per inclusion criteria given in Tables 1A and 1B<sup>12-24</sup> respectively were included in the study.

The fungi were isolated from blood, body fluids [ascitic fluid, pleural fluid, cerebrospinal fluid (CSF)], respiratory samples [sputum, endotracheal aspirate, bronchoalveolar lavage (BAL) fluid], urine, pus, fine needle aspiration cytology and surgical drain fluid. The clinical samples were processed in the Department of Microbiology.

The blood sample and body fluids were collected under aseptic conditions in BACTEC culture vials. In CSF sample, minimum of 5 mL was collected in a sterile container. All samples were transported to the laboratory in robust, leak proof sterile containers after putting identification number and name along with requisition slip.

### Sample processing

On direct microscopy, samples were examined by preparing either wet mount preparation or potassium hydroxide preparation (depending upon the nature of sample) to study the morphology of fungus. For CSF, India ink preparation and rapid cryptococcal antigen detection test was done.

**Table 1A: Criteria for diagnosis of fungal infection**


---

Blood <sup>12,13</sup>
Isolation of <i>Candida</i> species on blood culture
Isolation of <i>Cryptococcus neoformans</i> on blood culture
Ascitic fluid <sup>14,15</sup>
Isolation of <i>Candida</i> species on ascitic fluid culture
Pleural fluid <sup>16</sup>
Isolation of any type of fungus on pleural fluid culture
Cerebrospinal fluid <sup>13</sup>
India ink preparation positive for <i>Cryptococcus neoformans</i>
Detection of Cryptococcal antigen
Isolation of any type of fungus on CSF culture
Endotracheal aspirates <sup>17,18</sup>
Isolation of <i>Aspergillus</i> species from endotracheal aspirate culture
Bronchoalveolar lavage <sup>17,18</sup>
Isolation of <i>Aspergillus</i> species on BAL culture
Urine <sup>19,20</sup>
Isolation of <i>Candida</i> species on urine culture with Candiduria $\geq 10^4$ colony forming units/ml
Pus <sup>21</sup>
Isolation of any type of fungus on pus culture
Fine needle aspiration <sup>22</sup>
Isolation of any type of fungus on culture of fine needle aspirates

---

**Table 1B: Criteria for diagnosis of fungal colonization**


---

Sputum <sup>23</sup>
Isolation of <i>Candida</i> species on sputum culture
Endotracheal aspirate <sup>23</sup>
Isolation of <i>Candida</i> species from endotracheal aspirate culture
Bronchoalveolar lavage <sup>23</sup>
Isolation of <i>Candida</i> species on BAL culture
Surgical drain fluid <sup>24</sup>
Isolation of <i>Candida</i> species on surgical drain fluid culture

---

The samples for fungal culture were inoculated on four tubes of Sabouraud's dextrose agar (SDA). The specimens were inoculated on 4 tubes of SDA (2 with cycloheximide and 2 without cycloheximide) and incubated at 25 °C and 37 °C. SDA was examined daily for first week and twice a week for subsequent 4 weeks. Growth obtained was identified on basis of rate of growth, color, texture, pigmentation and morphological details. Lactophenol cotton blue

mount was prepared and seen in 40× magnification on the microscope.

Urine samples received for aerobic culture were inoculated on blood agar. The fungus isolated was identified by standard protocols.<sup>25</sup> All isolates of candida from urine and pus were pure or predominant isolates.

#### **Statistical analysis**

Baseline continuous variables with normal distribution were compared using unpaired

t-test; discrete variables were compared using Z-test for proportions. All tests were two-tailed; a p-value less than or equal to 0.05 was considered statistically significant. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 16.

## RESULTS

Of the 110 patients enrolled in the study, 91 (82.7%) had fungal infection, whereas 19 (17.3%) had fungal colonization. The mean age of patients with fungal infection and fungal

colonization were comparable (Table 2A;  $p=0.1590$ ). The demographic details of patients and critical care section distribution of patients is given in Table 2A. The underlying critical illness among patients with fungal infection admitted in surgical and medical critical care section is given in Table 2B.

The mean ICU stay before the isolation of fungus in the fungal infection and colonization groups were 9.3 (range 1- 41) days and 5.1 (range 1-14) days respectively with no statistically significant difference (Table 2A).

**Table 2A: Demographic details of patients with fungal infection and colonization**

Variable	Fungal infection (n=91)	Fungal colonization (n=19)	Total (n=110)
Age (years)*	51.2 ± 17.0	45.1 ± 17.3	50.1 ± 17.1
Males†	56 (61.5)	15 (79.0)	71 (64.6)
<i>Medical critical care section</i>			
Medical ICU†	17 (18.7)	7 (36.8)	24 (21.8)
Pulmonary Critical Care Unit†	22 (24.2)	6 (31.6)	28 (25.4)
Stroke ICU†	9 (9.9)	2 (10.5)	11 (10)
<i>Surgical critical care section</i>			
Surgery ICU†	31 (34.1)	3 (15.8)	34 (30.9)
Neurosurgery ICU†	12 (13.2)	1 (5.3)	13 (11.8)

\* data are expressed as mean ± SD

† data are expressed as No. (%)

n = number of patients; ICU = intensive care unit; SD = standard deviation

**Table 2B: Underlying critical illness in patients with fungal infection and colonization**

Diagnosis	Medical critical care section		Surgical critical care section	
	Fungal infection (n=48) No. (%)	Fungal colonization (n=15) No. (%)	Fungal infection (n=43) No. (%)	Fungal colonization (n=4) No. (%)
Central nervous system disease	12 (25)	2 (13.3)	1 (2.3)	0 (0)
Respiratory disease	11 (22.9)	10 (66.6)	1 (2.3)	0(0)
Gastrointestinal disease	10 (20.8)	0 (0)	13 (30.2)	01(25)
Malignancy	5 (10.4)	0 (0)	4 (9.3)	0 (0)
Infection	4 (8.3)	1 (6.6)	6 (13.9)	0 (0)
Trauma	3 (6.2)	0 (0)	17 (39.5)	3 (75)
Cardiovascular system disease	2 (4.1)	0 (0)	1 (2.3)	0 (0)
Genitourinary disease	1 (2.1)	2 (13.3)	0 (0)	0 (0)

n = number of patients

**Table 3: Presenting complaints and clinical signs in patients with fungal infection and colonization**

Clinical manifestation	Fungal infection	Fungal colonization
	(n=91) No. (%)	(n=19) No. (%)
<b>Symptoms</b>		
Fever	33 (36.3)	8 (42.1)
Cough	13 (14.3)	8 (42.1)
Breathlessness	18 (18.8)	11 (57.9)
Chest pain	5 (5.5)	1 (5.3)
Pain abdomen	24 (26.4)	0 (0.0)
Vomiting	20 (22.0)	4 (21.0)
Abdominal distension	8 (8.8)	0 (0.0)
Altered sensorium	27 (29.7)	7 (36.8)
Decreased urine output	8 (8.8)	5 (26.3)
<b>Signs</b>		
Jaundice	5 (5.5)	1 (5.3)
Pallor	20 (22.0)	7 (36.3)
Cyanosis	2 (2.2)	2 (10.5)
Clubbing	1 (1.1)	0 (0.0)
Icterus	8 (8.8)	2 (10.5)
Lymphadenopathy	0 (0.0)	0 (0.0)
Oedema	8 (8.8)	3 (15.8)
Raised jugular venous pressure	3 (3.3)	4 (21.0)

n = number of patients

The presenting symptoms and clinical signs observed most frequently in patients with fungal infection or fungal colonization are given at Table 3.

### Fungal infections

The most common fungus isolated in patients with fungal infections was *Candida* (n=85, 93.4%) patients, followed by *Aspergillus flavus* (3.3%) (Table 4). Among the *Candida*, most common isolates were *non-albicans Candida* spp. (61/85, 71.8%) whereas, *Candida albicans* constituted (24/85, 28.2%).

Among the *non-albicans Candida* spp., *Candida tropicalis* was most common isolate (52/61, 85.2%) patients followed by *non-albicans Candida* undifferentiated spp. (4.9%), *Candida guilliermondii* (3.2%), *Candida krusei*

(3.2%), *Candida parapsilosis* (3.2%) and *Candida stellatoidea* (1.6%) (Table 4).

The most common specimens yielding fungal infections were urine in (n=68, 74.7%), followed by blood (n=17, 20.8%), BAL fluid (2.2%), sputum endotracheal aspirate, cerebrospinal fluid, and pleural fluid (1.1% each). In 2 patients, *C. tropicalis* was isolated from both blood and urine respectively (Table 5A). In patients with urinary tract fungal infection, the most common fungus isolated was *C. tropicalis* (n=45, 66.2%), followed by *C. albicans* (n=17, 25%), *non-albicans Candida* undifferentiated spp. (4.4%), *C. krusei* (2.9%) and *C. stellatoidea* (1.5%). Among the patients with blood stream fungal infections, most common fungus isolated was *C. tropicalis* (n=9, 47.4%), followed by *C. albicans* (n=6, 31.6%), *C. guilliermondii* (10.5%), *C.*

**Table 4: Distribution of fungal isolates in patients with fungal infection and colonization**

Fungus	Fungal infection (n=91) No. (%)	Fungal colonization (n=19) No. (%)
<i>Candida</i>	85 (93.4)	19 (100)
<i>Candida albicans</i>	24 (28.2)	3 (15.8)
Non-albicans <i>Candida</i>	61 (71.7)	16 (84.2)
<i>C. tropicalis</i>	52 (85.2)	12 (63.1)
non-albicans <i>Candida</i> undifferentiated spp.	3 (4.9)	
<i>C. guilliermondii</i>	2 (3.2)	1 (5.3)
<i>C. krusei</i>	2 (3.2)	
<i>C. parasilosis</i>	1 (1.6)	-
<i>C. stellatoidea</i>	1 (1.6)	3 (15.8)
<i>Aspergillus flavus</i>	3 (3.3)	-
<i>Cryptococcus</i>	1 (1.1)	-
<i>Mucor species</i>	1 (1.1)	-
<i>Trichosporon beigelli</i>	1 (1.1)	-

n = number of patients

*parasilosis* (5.3%) and *Trichosporon beigelli* (5.3%).

### Fungal colonization

The most common fungus isolated from fungal colonization was *Candida tropicalis* in (n=12, 63%) patients, followed by *Candida albicans* and *Candida stellatoidea* (15.8 % each, and *Candida guilliermondii* (5.3%) (Table 4). The specimens in patients with fungal colonization were sputum, endotracheal aspirate, BAL fluid (n=6, 31.6% each) and surgical drain fluid (abdomen) (n=1, 5.2%) (Table 5B).

### Critical care setting-related risk factors

In the critical care setting-related risk factors in patients with fungal infections, the most common factor was presence of urinary catheter (85.7%). The other risk factors were central line insertion (81.3%), mechanical ventilation (52.7%), use of corticosteroids (23.1%), total parenteral nutrition (6.6%) and peritoneal dialysis (3.3%) (Table 6).

The number of patients with central line insertion (p<0.008) and urinary catheter (p<0.05) were significantly more in fungal

infection group whereas, those with peritoneal dialysis (p<0.05) were significantly more in fungal colonization group (Table 6). However, there was no significant difference in the mean duration of presence of these risk factors in both the groups.

Among underlying comorbid conditions, diabetes mellitus was present in 28.6% of patients with fungal infection and 26.3% of patients with fungal colonization with no statistically significant difference. Nine patients with fungal infections had underlying malignancy (Table 6).

The preference of empirical antibiotics in the critically ill patients was at the discretion of the treating clinician, which was modified in the course of hospitalization depending on bacterial culture sensitivity patterns. The use of antibiotics was present in all patients in fungal infection and fungal colonization groups. The most common antibiotic group used in patients with fungal infections was ureidopenicillins (57.1%), followed by 3<sup>rd</sup> generation cephalo-sporins (48.3%), glycopeptides (47.2%), carbapenems (46.1%)

**Table 5A: Specimen-wise distribution of isolates in patients with fungal infection (n=91)**

Specimen	Fungal infection No. (%)	Fungus type	
		Isolate	No. (%)
Urine*	68 (74.7)	<i>C. tropicalis</i>	45 (66.2)
		<i>C. albicans</i>	17 (25)
		non- <i>albicans</i> <i>Candida</i> undifferentiated spp.	3 (4.4)
		<i>C. krusei</i>	2 (2.9)
		<i>C. stellatoides</i>	1 (1.5)
Blood*	19 (20.9)	<i>C. tropicalis</i>	9 (47.4)
		<i>C. albicans</i>	6 (31.6)
		<i>C. guilliermondi</i>	2 (10.5)
		<i>C. parapsilosis</i>	1 (5.3)
		<i>Trichosporon beigelli</i>	1 (5.3)
Bronchoalveolar lavage	2 (2.2)	<i>Aspergillus flavus</i>	1
		<i>Mucor species</i>	1
Sputum	1 (1.1)	<i>C. tropicalis</i>	1
Endotracheal aspirate	1 (1.1)	<i>Aspergillus flavus</i>	1
Cerebrospinal fluid	1 (1.1)	<i>Cryptococcus neoformans</i>	1
Pleural fluid (chest tube)	1 (1.1)	<i>C. albicans</i>	1

\* *C. tropicalis* was isolated from both blood and urine in 2 patients respectively

n = number of patients

**Table 5B: Specimen distribution in patients with fungal colonization (n=19)**

Specimen	Fungal colonization No. (%)	Fungus type	
		Isolate	No.
BAL fluid	6 (31.6)	<i>C. tropicalis</i>	3
		<i>C. albicans</i>	1
		<i>C. stellatoides</i>	1
		<i>C. guilliermondi</i>	1
Sputum	6 (31.6)	<i>C. tropicalis</i>	3
		<i>C. albicans</i>	1
		<i>C. stellatoides</i>	2
Endotracheal aspirate	6 (31.6)	<i>C. tropicalis</i>	5
		<i>C. albicans</i>	1
Surgical drain fluid	1 (5.2)	<i>C. tropicalis</i>	1

BAL = bronchoalveolar lavage

**Table 6: Critical care setting risk factors and underlying co-morbid conditions in patients with fungal Infection and colonization**

Risk factors	Fungal infection	Fungal colonization	p-value
	(n=91) No. (%)	(n=19) No. (%)	
Urinary catheterization	78 (85.7)	12 (63.2)	< 0.05
Central line insertion	74 (81.3)	9 (47.4)	< 0.05
Respiratory ventilation	48 (52.7)	12 (63.2)	
Corticosteroid use	21 (23.1)	4 (21.1)	
Total parenteral nutrition	6 (6.6)	0 (0.0)	
Peritoneal dialysis	3 (3.3)	12 (63.2)	< 0.05
Underlying co-morbid conditions			
Diabetes Mellitus	26 (28.6)	5 (26.3)	
Malignancy	9 (9.9)	0 (0.0)	
HIV/AIDS	0 (0.0)	1 (5.3)	

n = number of patients; HIV= human immunodeficiency virus; AIDS= acquired immunodeficiency syndrome

and nitroimidazole (42.9%). However use of aminopenicillins, 4<sup>th</sup> generation cephalosporins, first generation fluoroquinolones, lincosamide antibiotics, macrolide antibiotics and oxazolidinone anti-biotics was more common in patients with the fungal colonization.

The duration of usage of lincosamide (clindamycin) (mean duration  $10.8 \pm 2.5$  days) and macrolide antibiotics (mean duration  $7.0 \pm 2.8$  days) was significantly higher in patients with fungal infections as compared to fungal colonization ( $p < 0.05$ ).

In fungal infections caused by *Candida albicans* as compared to non-*albicans Candida* species, there was no statistically significant difference among the mean ICU stay before isolation of fungus, ICU related-risk factors like use of corticosteroids, central line insertion, urinary catheter, respiratory ventilation, peritoneal dialysis, total parenteral nutrition and presence of underlying diabetes mellitus or malignancy.

However, there was a statistical trend favouring use of corticosteroids in *Candida albicans* group (mean duration  $13.3 \pm 7.5$  days) as compared to non-*albicans Candida* group (mean duration  $6.5 \pm 5.1$  days) ( $p = 0.05$ ). In

antibiotics used in both *Candida albicans* and non-*albicans Candida* group, uriedopenicillins (58.3% Vs 62.3%) were the commonly used antibiotics, followed by third generation cephalosporins (50% Vs 52.5%), carbapenems (41.7% Vs 52.5%), glycopeptides (50% Vs 50.8%) and nitroimidazole (37.5% Vs 49.2%) respectively with no significant difference between the two groups.

Nevertheless, in the duration of use of antibiotics in the critical care setting, there was a significant difference in the uriedopenicillins with a mean duration of  $9.1 \pm 3.9$  days in *Candida albicans* group as compared to  $6.1 \pm 4.6$  days in non-*albicans Candida* group ( $p < 0.05$ ).

## DISCUSSION

In this study, the most common fungi isolated in patients with fungal infection admitted in our critical care setting were *Candida* spp. (93.4%), followed by *Aspergillus* spp (3.3%). The predominance of *Candida* spp in nosocomial patients especially in the critical care setting is in consonance with a large multi-centric study done in United States, Canada, South America and Europe as part of international surveillance

program for fungal infections.<sup>26,27</sup> Similarly, the presence of *Aspergillus* spp. has also been documented as an adjunct cause of fungal infections in critically ill patients in the United States.<sup>28</sup>

Among the *Candida* species, most common fungi isolated in patients with fungal infections (including blood stream as well as urinary tract infections) were *non-albicans Candida* species (71.7%) in our study. This is also consistent with emergence of predominance of *non-albicans Candida* species all over the world.<sup>26,27</sup> In a study<sup>2</sup> undertaken in United States, reported the *non-albicans Candida* as emerging pathogens as cause of fungaemia. In another study<sup>29</sup> done in Italy, an increase in the *non-albicans Candida* species causing blood stream infections in a medical and surgical population has been reported during a 5-year period.

Among the *non-albicans Candida* species, *Candida tropicalis* was most common isolate in our study (85.2%). The preponderance of *Candida tropicalis* is consistent with observation in a study from Chandigarh.<sup>30</sup> Similarly, another retrospective study<sup>31</sup> done in Delhi reported *C. tropicalis* as most common cause of candidaemia. A recent case study<sup>10</sup> on 7 patients has also highlighted the emergence of newer non-albicans *Candida* like *Candida sake* in ICU patients. Another study<sup>8</sup> from Dehradun in a relatively smaller patient population has shown contrary results as compared to other centers of our country.<sup>8</sup> This study showed a predominance of *Candida albicans* in forty one patients. However, there were 13 neonates in the 41 patients enrolled in this study.

In our study, the most common site or specimen of fungus isolation in patients with fungal infection was urine (74.7%) followed by blood (20.8%). *C. tropicalis* was most common isolate from urine as well as from blood. Similar findings were observed in 2 recent studies of

nosocomial urinary tract infection from our country.<sup>7,10</sup> The age of the patients with fungal infections or fungal colonization in our study ranged from 18 to 86 years; the mean age of patients with fungal infection was  $51.2 \pm 17.0$  years. A study<sup>5</sup> from Delhi reported a similar range of 18 years to 80 years with a mean of 43.5 years.<sup>5</sup> Male predominance was noted in 61.5% patients. The results were consistent with the study<sup>6</sup> done in South India in which male predominance was reported in 71.2% in patients of blood stream *Candida* infections.

The mean ICU stay before the fungus isolation in patients with fungal infections in our study was found to be 9.3 days (range 1-41 days). In a study<sup>32</sup> from Greece, the mean time from ICU admission to the isolation of *Candida* from blood specimens was reported to be 9 days (range 5-11 days). In another study<sup>5</sup> from Delhi, the mean stay of 14.9 days with a range of 4-42 days was comparable with our study.

In our study, various ICU related risk factors like use of antibiotics, urinary catheterization, central line insertion, mechanical ventilation, use of steroids, total parenteral nutrition and peritoneal dialysis were compared in fungal infections in relation to fungal colonization. The use of central line insertion and urinary catheter were significantly more in patients with fungal infection as compared to those having fungal colonization. In a study<sup>5</sup> from Delhi, antibiotics, mechanical ventilation and central catheters were likewise found to be significantly related to candidaemia. In another study<sup>6</sup> from Kolkata, probable risk factors determined for fungaemia were intensive care unit stay, antibiotic therapy, central line, urinary catheter, ventilator, malignancy and abdominal surgery.

The use of antibiotics was present in all patients with fungal infections and colonization in our study. The most common antibiotic group used in patients with fungal infections was

uriedopenicillin, followed by third generation cephalosporins, glycopeptides, carbapenems and nitroimidazole. This probably was related to various underlying critical surgical and medical conditions. However, the preference of empirical antibiotics in the critically ill patients was at the discretion of the treating clinician.

In our study, *Candida albicans* group had no statistically significant difference in the mean ICU stay, ICU-related risk factors like use of steroids, central line insertion, urinary catheter, respiratory ventilation, peritoneal dialysis, total parenteral nutrition and presence of underlying diabetes mellitus or malignancy as compared to *non-albicans Candida* species.

On the other hand, in a study from United States, factors associated with blood stream infections (BSI) due to *non-albicans Candida* species were compared with *Candida albicans* BSIs in ICU patients.<sup>33</sup> It was observed that central venous catheter exposure was associated with increased risk of BSI due to *non-albicans Candida* species and total parenteral nutrition was associated with a decreased risk of BSIs due to *non-albicans Candida* species compared with *Candida* species. However, in supplementary study it was concluded that there are multiple common risk factors for both *albicans* and *non-albicans Candida* BSIs and it is not possible to differentiate between these two groups based on clinical characteristics alone.<sup>34</sup>

In conclusion, to the best of our knowledge, our study is the largest surveillance study enrolling 110 patients in an adult medical and surgical critical care setting with documented fungal infection and fungal colonization over a period of one year from our country. The emergence of *non-albicans Candida* similar to the trends in the western countries should be a cause of concern in our country. The major risk

factors were use of antibiotics, urinary catheter and central line insertion.

Proper surveillance of fungal pathogens is important to improve quality of care in ICU. There is an urgent need for sensitization of health care personnel to evolve preventive risk factor protocols as part of standard of care to control the surge of fungal infections in critical care settings.

---

## REFERENCES

---

1. Jorda-Marcos R, Alvarez- Lerma F, Jurado M, Palomar M, Nolla-Salas J, Leon MA, et al Risk factors for candidemia in critically ill patients: a prospective surveillance study. *Mycoses* 2007;50:302-10.
2. Nguyen MH, Peacock JE Jr, Morris AJ, Tanner DC, Nguyen ML, Snyderman DR, et al. The changing face of candidemia: emergence of non-*Candida albicans* species and antifungal resistance. *Am J Med* 1996;100:617-23.
3. Kobayashi CC, de Fernandes OF, Mirande KC, de Sousa ED, Silva Mdo R. Candiduria in hospital patients: a prospective study. *Mycopathologia* 2004;158: 49-52.
4. Charles PE, Dalee F, Aube H, Doise JM, Quenot JP, Aho LS, et al. *Candida* spp. colonization significance in critically ill medical patients: a prospective study. *Intensive Care Med* 2005;31:393-400.
5. Sahni V, Aggarwal SK, Singh NP, Anuradha S, Sidakkar S, Wadhwa A, et al. Candidemia--an under-recognized nosocomial infection in Indian hospitals. *J Assoc Physicians India* 2005;53:607-11.
6. Shivaprakasha S, Radhakrishnan K, Karim PM. *Candida* Spp. other than *Candida albicans*: a major cause of fungaemia in a tertiary care centre. *Indian J Med Microbiol* 2007;25:405-7.
7. Singla N, Gulati N, Kaistha N, Chander J. *Candida* colonization in urine samples of ICU patients: determination of etiology, antifungal susceptibility testing and evaluation of associated risk factors. *Mycopathologia* 2012;174:149-55.
8. Kotwal A, Biswas D, Sharma JP, Gupta A, Jindal P. An observational study on the epidemiological

- and mycological profile of Candidemia in ICU patients. *Med Sci Monit* 2011;17:CR663-8.
9. Jain M, Dogra V, Mishra B, Thakur A, Loomba PS, Bhargava A. Candiduria in catheterized intensive care unit patients: emerging microbiological trends. *Indian J Pathol Microbiol* 2011;54:552-5.
  10. Juneja D, Borah AK, Nasa P, Singh O, Javeri Y, Dang R. Candida sake candidaemia in non-neutropenic critically ill patients: a case series. *Crit Care Resusc* 2011;13:187-91.
  11. Capoor MR, Nair D, Deb M, Verma PK, Srivastava L, Aggarwal P. Emergence of non-albicans Candida species and antifungal resistance in a tertiary care hospital. *Jpn J Infect Dis* 2005;58:344-8.
  12. Richardson MD, Carlson P. Culture and non culture based diagnosis for Candida species. In: Calderone RA, editor. *Candida and Candidiasis*. Washington: AMS; 2001. p. 388.
  13. Perfect JR. *Cryptococcus neoformans*. In: Mandell GL, Bennett EJ, Dolin R, editors. *Principles and practice of infectious diseases*. New York: Churchill Livingstone; 2005. p. 2997-12.
  14. Edwards JE Jr. *Candida Species*. In: Mandell GL, Bennett EJ, Dolin R, editors. *Principles and Practice of Infectious Diseases*. New York: Churchill Livingstone; 2005.p.2938-57.
  15. Dupont H, Paugam-Burtz C, Muller-Serieys C, Fierobe L, Chosidow D, Marmuse JP, et al. Predictive factors of mortality due to polymicrobial peritonitis with Candida isolation in peritoneal fluid in critically ill patients. *Arch Surg* 2002;137:1341-6.
  16. Shiann CH, Kuan YC, Po-Ren H, Kwen-Tay L, Pan-Chyr Y. Fungal empyema thoracis: an emerging clinical entity. *Chest* 2000;117:1672-8.
  17. Vanderwonde KH, Blot SI, Depuydt P, Benoit D, Temmerman W, Colardyn F, et al. Clinical relevance of *Aspergillus* isolation from respiratory tract samples in critically ill patients. *Crit Care* 2006;10:132.
  18. Horvath JA, Dummer S. The use of respiratory-tract cultures in the diagnosis of invasive pulmonary aspergillosis. *Am J Med* 1996;100:171-8.
  19. Sellami A, Sellami H, Makni F, Bahloul M, Cheikh-Rouhou F, Bouaziz M, et al. Candiduria in intensive care unit: significance and value of yeast numeration in urine. *Ann Fr Anesth Reanim* 2006;25:584-8.
  20. Chabasse D. Yeast count in urine. Review of the literature and preliminary results of a multicenter prospective study carried out in 15 hospital centers. *Ann Fr Anesth Reanim* 2001;20:400-6.
  21. Sundaram C, Lakshmi V. Pathogenesis and pathology of brain abscess. *Indian J Pathol Microbiol* 2006;49:317-26.
  22. Williamson JD, Silverman JF, Mallak CT, Christie JD. Atypical cytomorphologic appearance of *Cryptococcus neoformans*: a report of five cases. *Acta Cytol* 1996;40:363-70.
  23. el-Ebiary M, Torres A, Fàbregas N, de la Bellacasa JP, González J, Ramirez J, et al. Significance of the isolation of *Candida* species from respiratory samples in critically ill, non neutropenic patients. An immediate histologic study. *Am J Respir Crit Care Med* 1997;156:583-90.
  24. Zoragoza R, Peman J, Salavert M. Is the use of antifungal management advisable in critical patients with positive isolation of *Candida* spp. from intraabdominal clinical samples? *Rev Iberoam Micol* 2008;25:203-7.
  25. Toya SP, Schraufnagel DE, Tzelepis GE. Candiduria in intensive care units: association with heavy colonization and candidaemia. *J Hosp Infect* 2007;66:201-6.
  26. Pfaller MA, Jones RN, Doern GV, Sader HS, Hollis RJ, Messer SA. International surveillance of bloodstream infections due to *Candida* species: frequency of occurrence and antifungal susceptibilities of isolates collected in 1997 in the United States, Canada, and South America for the SENTRY Program. The SENTRY Participant Group. *J Clin Microbiol* 1998;36:1886-9.
  27. Pfaller MA, Jones RN, Doern GV, Fluit AC, Verhoef J, Sader HS, Messer SA, Houston A, Coffman S, Hollis RJ. International surveillance of blood stream infections due to *Candida* species in the European SENTRY Program: species distribution and antifungal susceptibility including the investigational triazole and echinocandin agents. SENTRY Participant Group (Europe). *Diagn Microbiol Infect Dis* 1999;35:19-25.

28. Zilberberg MD, Shorr AF. Fungal infections in the ICU. *Infect Dis Clin North Am* 2009;23:625-42.
29. Bassetti M, Righi E, Costa A, Fasce R, Molinari MP, Rosso R, et al. Epidemiological trends in nosocomial candidemia in intensive care. *BMC Infectious Diseases* 2006;6:21.
30. Chakrabarti A, Chatterjee SS, Rao KL, Zameer MM, Shivaprakash MR, Singhi S, et al. Recent experience with fungaemia: change in species distribution and azole resistance. *Scand J Infect Dis* 2009;41:275-84.
31. Kothari A, Sagar V. Epidemiology of candida bloodstream infections in a tertiary care institute in India. *Indian J Med Microbiol* 2009;27:171-2.
32. Dimopoulos G, Karabinis A, Samonis G, Falagas ME. Candidaemia in immunocompromised and immunocompetent critically ill patients: a prospective comparative study. *Eur J Clin Microbiol Infect Dis* 2007;26:377-84.
33. Chow JK, Golan Y, Ruthazer R, Karchmer AW, Carmeli Y, Lichtenberg D, et al. Factors associated with candidaemia caused by non-albicans *Candida* species versus *Candida albicans* in intensive care unit. *Clin Infect Dis* 2008;46:1206-13.
34. Chow JK, Golan Y, Ruthazer R, Karchmer AW, Carmeli Y, Lichtenberg DA, et al. Risk factors for albicans and non albicans candidemia in the intensive care unit. *Critical Care Med* 2008;36:1993-8.