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ISOLATION AND CHARACTERIZATION OF CANDIDA SPECIES IN ICU PATIENTS: A PROSPECTIVE OBSERVATIONAL STUDY FROM KUMAON REGION, UTTARAKHAND, INDIA

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ABSTRACT: Background: Fungi have emerged as major cause of human diseases since early 1980s. In hospitalized patients with serious underlying diseases and those having immunocompromised state, opportunistic fungal infections bring about a substantial increase in morbidity and mortality. **Aim and Objectives:** Isolation and characterization of Candida species in ICU patients of Dr. Susheela Tiwari Government Hospital, Haldwani, Uttarakhand. **Materials and Methods:** A prospective observational study was conducted for two years from Nov 2015 to Oct 2017 and 2323 samples were collected from suspected cases of Candida infection, admitted in ICU of Dr. Susheela Tiwari Government Hospital, Haldwani. Identification of Candida species was done by standard laboratory processes. **Results:** In the present study, out of 2323 clinical specimens received from different ICU's, 104 samples were found positive for Candida species. Majority of the patients were in the age group > 60 years (24.04%). We observed that Non-albicans Candida (NAC) species (67.3%) were more frequently encountered than *C. albicans* (32.7%). Among NAC, C. tropicalis was the most common species (61.4%). Maximum numbers of Candida species (81.73%) were isolated from urine samples. **Conclusion:** The global incidence of Candidiasis has risen steadily over the past few decades. NAC is emerging as a significant problem in hospitalized patients especially in ICU setup. Early speciation of Candida isolates will restrict the empirical use of antifungal agents, which will greatly help in making clinical decisions for the benefit of patients.

INTRODUCTION: Fungi have emerged as a major cause of human diseases since early 1980s [1, 2].

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Among the various risk factors for developing fungal infections, the most important ones are an ever-expanding population with immuno-compromised state.

Other risk factors include sepsis, surgical procedures, increasing use of broad-spectrum antibiotics, cytotoxic chemotherapies and transplantations [3, 4]. Intensive Care Units (ICU), which though typically represent only about 5% of

hospital beds, are host to more than 20% of hospital infections and harbor almost all the risk factors for opportunistic fungal infections [5, 6, 7]. Candida bloodstream infection (Candidemia) is a life-threatening affliction associated with intensive care unit (ICU) patients [8, 9]. Candida remains the most important cause of opportunistic mycoses worldwide. They are the sixth most common nosocomial pathogen and fourth most common cause of nosocomial sepsis according to the National Nosocomial Infection Surveillance system [10, 11]. Recent trends demonstrate a gradual change in its species distribution, with many countries experiencing a relative rise in the proportion of Non-albicans Candida (NAC) spp. like *Candida tropicalis*, *Candida parapsilosis*, *Candida glabrata* and *Candida krusei*. Also, NAC shows decreased *in-vitro* susceptibility to fluconazole as compared to *C. albicans* [12, 13]. In view of the geographical and temporal variation often observed in the species distribution of Candida, there is a need to investigate and monitor local epidemiological patterns of Candida infections in India [12]. So, our study was conceptualized to provide data for judicious administration of antifungal therapy in patients who are at risk or are suffering from candidiasis.

MATERIALS AND METHODS:

Study Design: A prospective observational study was conducted in ICU patients of Dr. Susheela Tiwari Government Hospital, Haldwani for two years from Nov 2015 to Oct 2017

Study Setting and Population: Samples were collected from suspected cases of Candida infection admitted in ICU of Dr. Susheela Tiwari Government Hospital, Haldwani. Candida isolated from the samples were subjected to speciation using the following techniques according to standard protocols [7] – KOH mount, Gram's stain, India Ink preparation, culture on Sabouraud's Dextrose Agar, Germ Tube test, Urea hydrolysis, Cornmeal Agar morphology (Dalmau plate technique), morphology in CHROM agar, Carbohydrate fermentation test, Carbohydrate assimilation test.

Sample size: Assuming an average rate of occurrence of Candidia isolates in ICU to be 50% and a margin of error of 2.3%, the expected sample size for this study was calculated to be 1872. Considering sample spoilage rate of 10%, minimum sample size came to be 2059 but we planned to include 2323 samples in our study to add more precision to the study.

Inclusion Criteria: Clinical samples from suspected Candidiasis, who were critically ill and admitted in the Medical (MICU), Surgical (SICU), Pediatric (PICU), and Anaesthesia (AICU) ICU's.

Exclusion Criteria: Patients previously treated with or were on antifungal drug therapy.

Ethical Clearance: Study protocol was approved by Institutional Ethical Committee (IEC) of Government Medical College, Haldwani via letter no. 286/GMC/IEC/2015/Reg.No.251/IEC/R-19-09-2015

Statistical Analysis: Collected data was coded appropriately, entered in Microsoft Excel (MS Excel) spreadsheet and later cleaned for any possible errors in SPSS Statistics for Windows v. 16.0 (IBM Corp., Armonk, NY). Categorical data are presented as percentage. Descriptive analysis of categorical data is presented as frequencies and percentages.

RESULTS:

Distribution of Different Samples in ICU's: A total of 2323 clinical specimens were collected from ICU during the study period, of which majority of the samples were urine 64.3% followed by blood 13.4% **Table 1.**

TABLE 1: DISTRIBUTION OF DIFFERENT SAMPLES IN ICU'S

Samples	Number (%)
Urine	1494 (64.31)
Blood	312 (13.43)
Pus	274 (11.79)
CSF	117 (5.03)
Peritoneal Fluid	68 (2.92)
Pleural Fluid	58 (2.49)
Total	2323

Age & Gender-wise Distribution of *C. albicans* & NAC: Maximum number of Candida, 25 (24.04%) were isolated from the patients in the geriatric age group of >60 years followed by 51-60 age group. Male to female ratio was 1.8:1 as total male were 67 and female were 37 **Table 2.**

TABLE 2: AGE & GENDER-WISE DISTRIBUTION OF *C. ALBICANS* & NAC

	C. albicans		NAC		
Age	**M**	**F**	**M**	**F**	**Total N (%)**
0-10	4	2	4	4	14 (13.46)
11-20	0	3	1	3	07 (6.74)
21-30	2	2	4	2	10 (9.62)
31-40	2	1	0	3	06 (5.76)
41-50	4	2	10	4	20 (19.23)
51-60	5	2	12	3	22 (21.15)
>60	4	2	15	4	25 (24.04)
Total N (%)	21 (20.19)	14 (13.46)	46 (44.23)	23 (22.11)	104

Different Candida species Isolated from ICU Patients: Total samples positive for Candida species were 104, of which 34 (32.69%) and 70 (67.30%) were positive for *C. albicans* and Non-albicans Candida (NAC) respectively **Fig. 1.**

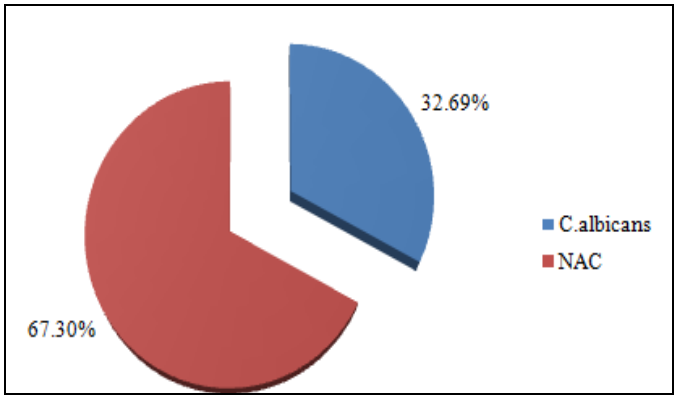

FIG. 1: PIE DIAGRAM SHOWING DIFFERENT CANDIDA SPP. ISOLATED FROM ICU PATIENTS

Distribution of *C. albicans* and NAC in Different ICUs: Non-albicans Candida species were more frequently detected in all critical units as compared to *C. albicans* **Fig. 2.**

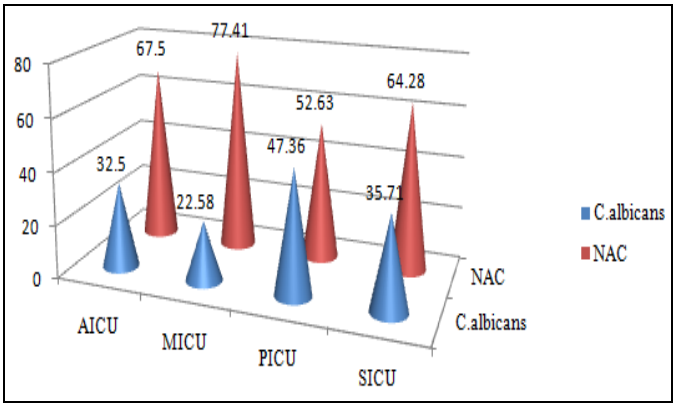

FIG. 2: BAR DIAGRAM SHOWING DISTRIBUTION OF *C. ALBICANS* AND NAC IN DIFFERENT ICUS

Distribution of NAC Species in Different ICU's: Among NAC species, *C. tropicalis* was predominantly isolated from all the ICU's **Table 3.**

TABLE 3: DISTRIBUTION OF CANDIDA SPP. IN DIFFERENT ICU'S

Different ICU	CT N (%)	CK N (%)	CG N (%)	CD N (%)	CP N (%)	Total N (%)
AICU	18 (66.66)	03 (11.11)	02 (7.40)	04 (14.81)	00 (00.00)	27 (38.57)
MICU	16 (66.66)	02 (8.33)	02 (8.33)	02 (8.33)	02 (8.33)	24 (34.28)
PICU	06 (60.00)	02 (20.00)	00 (00.00)	01 (10.00)	01 (10.00)	10 (14.28)
SICU	03 (33.33)	01 (11.11)	03 (33.33)	01 (11.11)	01 (11.11)	09 (12.85)
Total	43 (61.43)	08 (11.42)	07 (10.00)	08 (11.42)	04 (5.71)	70

CT- *C. tropicalis*, CK- *C. krusei*, CG- *C. glabrata*, CD- *C. dubliniensis*, CP- *C. parapsilosi*.

Sample-wise Distribution of Candida species: Maximum no. of *C. albicans* and NAC were isolated from urine sample (81.73%) **Table 4.**

TABLE 4: SAMPLE-WISE DISTRIBUTION OF CANDIDA SPECIES

Candida Isolates	Urine N (%)	Pus N (%)	Blood N (%)	Peritoneal Fluid N (%)	Pleural Fluid N (%)	Total N (%)
C.albicans	25(73.52)	2 (5.88)	5(14.70)	2 (5.88)	0(0)	34(32.70)
NAC	60(85.71)	2(2.85)	2(2.85)	3(4.28)	3(4.28)	70(67.30)
Total N (%)	85(81.73)	4(3.84)	7(6.73)	5(4.80)	3(2.88)	10(100)

Among NAC, C. tropicalis (60%) was predominant species isolated from urine **Table 5.**

TABLE 5: DISTRIBUTION OF NAC SPP. IN DIFFERENT CLINICAL SAMPLES

Candida Isolates	Urine N (%)	Pus N (%)	Blood N (%)	Peritoneal Fluid N (%)	Pleural Fluid N (%)	Total N (%)
C. tropicalis	36(60)	2(100)	2 (100)	(33.3)	2(66.7)	43(61.4)
C. glabrata	7(11.7)	0(0)	0(0)	0(0)	0(0)	7(10)
C. krusei	7(11.7)	0(0)	0(0)	1(33.3)	0(0)	8(11.4)
C. dubliniensis	7 (11.7)	0(0)	0(0)	0(0)	1(33.3)	8 (11.4)
C. parapsilosis	3 (5)	0(0)	0(0)	1(33.3)	0(0)	4 (5.7)
Total N (%)	60(85.71)	2(2.89)	2(2.89)	3(4.28)	3(4.28)	70(100)

DISCUSSION: Candida species are the most common cause of fungal infections worldwide, leading to a range of mild muco-cutaneous to life-threatening invasive diseases. The risk of acquiring nosocomial infections in ICU patients is higher due to severity of the underlying illnesses and iatrogenic factors related to the high frequency of invasive procedures in them [14]. In the present study, out of 2323 clinical specimens received from different ICU's, 104 samples were found positive for Candida species. Majority of the patients were in the age group > 60 years (24.04%), this finding was in concordance with Gupta *et al* where maximum number of patients were in the age group of 60-69 years (22.6%) [15].

In contrast to this, Kaur *et al* found maximum patients in the age group of 21-30 years (46.6%) [16]. Candida infection affects both sexes and mainly extremes of ages, possibly due to the immaturity of the immune system in children and the waning of the immune response in the elderly [17]. In our study, male to female ratio was 1.8:1. Similar figure of 1.8:1 and 1.7:1 was reported by Leon *et al* and Gonzalez de *Molina et al.* [18, 19].

In the present study, we observed that NAC species (67.3%) were more frequently encountered than *C. albicans* (32.7%). The findings were in concordance with other studies in New Delhi, Ludhiana, and Punjab [16, 17, 20] which reported 61.2%, 71.8% and 60.8% of NAC isolates respectively. This was in contrast to the study conducted by Leroy O *et al* which showed a higher isolation (57.0%) of *C. albicans* as compared to NAC [21]. Among NAC, *C. tropicalis* was the most common species (61.4%) in our study which was in consistent to finding by Kaur *et al,* Singh T *et al* and Sharma *et al* [16, 17, 20] while in a study by Leroy O *et al* [21], *C. glabrata* was isolated more as compared to *C. tropicalis*. Maximum numbers of Candida species (81.73%) were isolated from urine samples. Similarly, Kaur *et al* and Singh T *et al* found most of Candida spp. from urine samples (39.8% and 74.7% respectively) [16, 17]. Whereas, Chaudhari B K *et al* found maximum numbers of Candida isolates from blood (74%) followed by urine (18%) [11]. In our study, *C. tropicalis* was most often isolated from urine (60%). This was similar to the findings by Kaur *et al,* Singh T *et al* and Sharma *et al* [16, 17, 20]. Geographical variation is recognized to be an important feature in the species distribution of candida. Worldwide, a shift in the species distribution of Candida from albicans to non-albicans has been noted. Various studies have correlated this shift with the increase in the use of fluconazole [22].

CONCLUSION: Candidiasis is emerging as a significant problem in hospitalized patients, especially in ICU set up. The present study highlights the predominance of NAC species colonization in ICU patients similar to the trends in the western countries. Some of the NAC species *e.g. C. tropicalis*, *C. krusei* and *C. glabrata* were intrinsically resistant to commonly used antifungal drug like Fluconazole. Therefore, potential clinical importance of early speciation of Candida isolates will be optimal use of antifungal agents. Also, this will open wider treatment options for the clinicians which will ultimately become beneficial for the patients.

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Limitations: Multicentric studies are required so that our findings can be generalized.

CONFLICT OF INTEREST: All authors have no conflict of interest.

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