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ORIGINAL RESEARCH

A study of *Candida albicans* and non-*albicans Candida* species isolated from various clinical samples and their antifungal susceptibility pattern

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Abstract

Background: *Candida* species are the most common cause of fungal infections worldwide. *Candida albicans* has been the most common causative agent until recent past but frequency of non-*albicans Candida* (NAC) species is on the rise. This changing epidemiology and increase in resistance to antifungal agents makes it important to identify *Candida* up to the species level and know its antifungal susceptibility pattern.

Aim: To provide data on *Candida* species prevalence and to highlight the need of speciation of *Candida* and its antifungal susceptibility testing.

Material and methods: For blood cultures, BacT/ALERT blood culture automated system (BioMérieux) was used. *Candida* was identified initially by direct microscopic examination of samples received and culture was done on SDA with antibiotic. Differentiation of *Candida albicans* and NAC species was done by germ tube test and final identification and antifungal susceptibility testing were done using Vitek 2 compact.

Result- The prevalence of *Candida* infection in this study is 1.58%. Out of total 100 *Candida* isolates, 25% were *C.albicans* and 75% were NAC. Among 75 non-*albicans Candida* spp.; *C.tropicalis* (46) forms the major isolate. Other NAC spp. included *C.hemulonii* (9), *C.glabrata* (6) & others (14). *C.albicans* is found to be more susceptible to fluconazole as compared to NAC spp. In this study NAC species showed comparatively reduced susceptibility to fluconazole and amphotericin B.

Conclusion: There is a significant epidemiological shift in candidiasis cases due to NAC species. Based on the present results and trends, it becomes essential to routinely identify *Candida* isolates up to species level, and detect evolving resistant strains by antifungal susceptibility testing wherever feasible.

Keywords: Non-*albicans Candida; Candida auris;* emerging infection; antifungal resistance

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Introduction

Candida species are the most common cause of fungal infections worldwide [1]. *C.albicans* is the most common causative agent of candidiasis; but its incidence is declining and the frequency of other non-*albicans Candida* (NAC) species is increasing [2]. The genus *Candida* consists of about 200 species and around 20 distinct *Candida* species are known to cause human disease. More than 90-95% of invasive disease is caused by 5 most common pathogens, namely: *C.albicans, C.tropicalis, C.glabrata, C.parapsilosis* and *C.krusei* [3, 4]. *Candida* being a significant opportunistic pathogen; causes a wide variety of infections in human; ranging from trivial intertriginous infection to fatal candidemia [5]. Studies from India have reported candidemia prevalence rates from 6-18% [6-10]. In India candidemia incidence varies from 0.24 to 34.3 patients/1,000 ICU admissions and mortality rate ranges from 35-45% [11-15].

Candida auris has recently set an alarming state worldwide with its rapid spread within hospitals and between hospitals worldwide. Due to its multidrug resistant nature and often misidentification; it causes a broad range of healthcare-associated invasive infections (HCAI). It forms an important cause of nosocomial outbreaks and factor contributing to the spread of *C.auris* is its propensity to persist on the surfaces of hospital rooms and on medical devices [16-18]. Recently, *C.auris* was found to be the second most prevalent species causing candidemia in a tertiary care trauma center in Delhi, India, warranting more effective infection control practices to prevent its spread [19].

Due to the close genetic relatedness with *C. haemulonii* complex, *C.auris* is often commonly misidentified as *C.haemulonii* in routine diagnostic laboratories using biochemical methods. In fact, commercially available biochemical-based tests, including API AUX 20C, VITEK-2 YST, BD Phoenix, and MicroScan, misidentifies *C.auris* as a wide range of *Candida* species and other genera. Misidentifications *as C.famata, C.sake*, *Rhodotorula glutinis*, *Rhodotorula mucilaginosa*, *Saccharomyces*, *C. catenulate*, *C.lusitaniae*, *C.guilliermondii* and *C. parapsilosis* have also been reported [20-22]. Recently, BioMérieux has updated the database [23-24] and inclusion of *C.auris* spectra in the VITEK-2 system has led to its correct identification.

Frequent use of antifungal agents like fluconazole for prophylaxis & therapy, use of broad spectrum antibiotics; has led to the change in the prevalence of the *Candida* species and emergence of less susceptible *Candida* species. Infections with NAC are on rise and there is increase in resistance to antifungal agents. Hence, this study is taken up to find out the distribution of different *Candida* species & provide detailed database on the prevalence, distribution and antifungal susceptibility pattern of the *Candida* isolates against common antifungal agents used in a tertiary care hospital. This would help in better understanding of present scenario.

Material and methods

This is a one year prospective study, which was conducted from August 2016 to July 2017 in the Department of Microbiology at Krishna Institute of Medical Science, Secunderabad, India; after obtaining clearance from ethics committee on 9 August 2016 - The KIMS Foundation and Research center (KFRC/EC/2016/57-09). Samples submitted to the microbiology laboratory like blood, pus, fluids, tissues, etc. from inpatients with symptoms and clinical manifestations suggestive of *Candida* infection were included in the study. It included all patients with positive culture showing pure growth of *Candida* admitted in intensive care units (ICU), Organ transplantation units & wards at KIMS Hospital, Secunderabad. Samples from out-patients department and samples like oral cavity wash, sputum, endotracheal secretions, bronchial wash, vaginal swabs & urine from in-patients were excluded from this study. All the consecutive samples and samples with isolation of *Candida* from two different contiguous sites were included till the sample size was met.

Fluid, pus or tissue biopsy from affected site; blood sample in case of disseminated infections were collected during the study period and they were processed and cultured based on standard microbiological guidelines. Preliminary tests included macroscopic examination of samples and direct microscopic examination by Gram's staining. Potassium hydroxide (KOH) mount and Gomori's methanamine silver (GMS) staining was done for tissues and deep seated specimen. For blood cultures, BacT/ALERT blood culture automated system (BioMérieux) was used. *Candida* was isolated by doing culture on 5% sheep blood agar (BA) and Sabouraud's dextrose agar (SDA) with antibiotic

(chloramphenicol). Preliminary speciation was carried using germ tube test (GTT) & culture on cornmeal agar (CMA) for observing chlamydospore formation. Finally isolated species were identified and confirmed using YST identification card of Vitek 2 compact system (BioMérieux). In Vitek, the identification level gives the confidence level with which an unknown bio pattern is compared. Various qualitative levels of identification (Excellent – 96-99% probability, Very good – 93-95%, Good – 89-92%, etc.) were assigned based on the numerical probability calculation. Isolates showing high confidence level were only included in this study. In case of rare species being identified, isolate was sent to referral mycology laboratory for final identification.

The antifungal susceptibility testing of all *Candida* isolates were done for fluconazole, voriconazole, amphotericin B, caspofungin and micafungin by using AST-YS07/08 card in VITEK 2 compact system [25-27]. The susceptibility to the above antifungal drugs is considered based on MIC values according to CLSI guidelines based on standard methods in document M27-A3 for macrobroth and microtitre yeast testing & M60 document [25, 28-30]. Final identification results were available in approximately 16-18 hours.

Results

KIMS is a 1000 bedded tertiary care hospital with its laboratory receiving samples from all specialties and super-specialties. Inpatients with symptoms and clinical manifestations suggestive of *Candida* infection admitted in ICU's, organ transplantation units & wards were included in this study. Positive cultures showing pure growth of *Candida* from samples of patients with high clinical suspicion along with other associated factors and co-morbidities were only included. All the patient samples wherein *Candida* was isolated as a part of normal commensal or forms a part of colonization were excluded from the study. Only paired blood culture samples were included in the study. Clinical correlation was done for all the patients included in the study.

Total number of samples (blood, pus, fluids, central line tips, tissues, etc.) received during the study period for culture and sensitivity was 6326. Culture positives out of total received samples were 1844 (29.1%). Among them, 100 were cultures positive for *Candida* species. Hence, the prevalence of *Candida* infection in the present study is 1.58%.

In this study of one year; only 25(25%) of the isolates were *Candida albicans* and rest 75(75%) of the isolates were NAC (Figure 1).

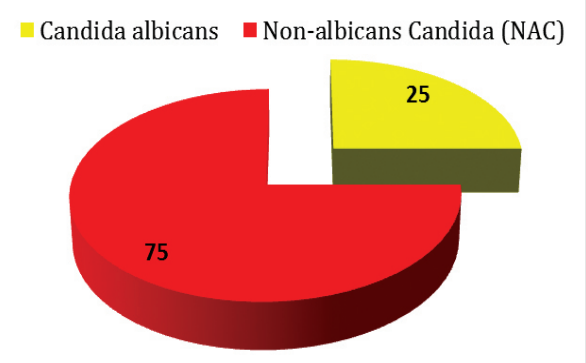

Figure 1: Percentage of *Candida* isolates.

Out of 75 NAC isolates (Figure 2), 46(61.33%) were *Candida tropicalis*, 9(12%) were *C.hemulonii*, 6(8%) were *C.glabrata*, 4(5.33%) *C.famata*, 4(5.33%) *C.parapsilosis*, 2(2.66%) were *C.guilliermondii*, 1(1.33%) was *C.auris* and others accounted for remaining 3(4%) which included one isolate each of *C.krusei, C.spherica* and *C.lusitaniae.*

The features of identification of *Candida spp.* and variation by Gram's stain, germ tube test (GTT), cut-streak culture on cornmeal agar (CMA) and by Vitek 2 is shown in Table 1.

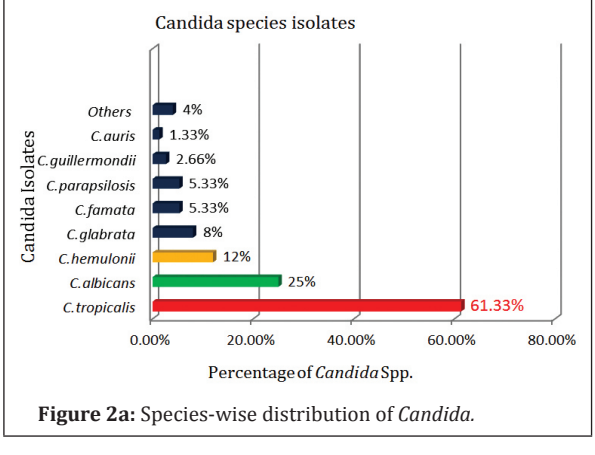

Figure 2a: Species-wise distribution of *Candida.*

Out of total 100 patients with candidiasis; 67(67%) were male and 33(33%) were female (Figure 3). The predominant age group (Figure 4) affected were adults 42% (>30yrs) and elderly 40% (>60yrs).

Table 1: Features of various *Candida* spp., on Gram's stain, germ tube test (GTT), cut-streak culture on CMA & Vitek.

S.No	Candida spp.	Gram's stain	GTT	CMA	Vitek	Variations
1.	*C.albicans* (25)	Spherical/ sub-spherical blastoconidia ~2-7×3-8µm	Positive	Production of pseudohyphae & chlamydospores mostly terminal	Identified as *C.albicans*	Nil
2.	*C.tropicalis* (46)	Spherical/ sub-spherical blastoconidia ~3-5.5×4-9µm	Negative	Abundant branched, long pseudohyphae with many ovoid blastoconidia	Identified as *C.tropicalis*	Nil
3.	*C.hemulonii* (9)	Ovoid to spherical blastoconidia ~3-5×3-6.5µm	Negative	No pseudohyphae produced Spherical to ovoid budding yeasts only	Identified as *C.hemulonii*	Nil
4.	*C.glabrata* (6)	Ovoid blastoconidia ~3.4×2.0µm	Negative	No pseudohyphae or chlamydospores produced Ovoid budding yeasts only	Identified as *C.glabrata*	Nil
5.	*C.famata* (4)	Ovoid blastoconidia ~3.5×2-3.5 µm	Negative	No pseudohyphae produced Spherical to ovoid budding yeasts only	Identified as *C.famata*	Nil
6.	*C.parapsilosis* (4)	Small spherical to ovoid blastoconidia ~2-3.5×3-4.5 µm	Negative	Abundant branched pseudohyphae with blastoconidia in small clusters arranged like "Spider colonies"	Identified as *C.parapsilosis*	Nil
7.	*C.guilliermondii* (2)	Spherical/ sub-spherical blastoconidia ~2-4×3-6 µm	Negative	Branched pseudohyphae with dense blastoconidia	Identified as *C.guilliermondii*	Nil
8.	*C.auris* (1)	Ovoid blastoconidia ~2-5×3-7µm	Negative	Budding yeast cells only. No Pseudohyphae	Identified as *C.auris* in blood	Misidentified as *C.famata* and *C.hemulonii* in other samples
9.	*C.krusei* (1)	Small ovoid blastoconidia ~2-5.5×4-11 µm	Negative	Abundant long, branched pseudohyphae with ovoid blastoconidia	Identified as *C.krusei*	Nil
10.	*C.lusitaniae* (1)	Ovoid blastoconidia ~1.5-6×2.5-10 µm	Negative	Abundant branched pseudohyphae with ovoid blastoconidia	Identified as *C.lusitaniae*	Nil

Among male and females; predominant age-group affected was 40-60 years in males whereas in females predominant age-group affected was 60-80yrs in women.

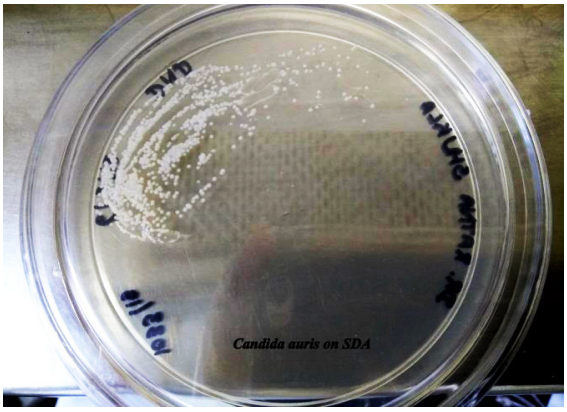

Figure 2b: *Candida auris* on SDA plate.

Figure 2c: *Candida auris* on blood agar.

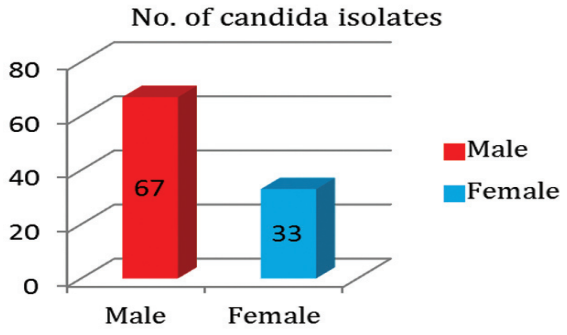

Figure 3: Gender-wise distribution of *Candida*.

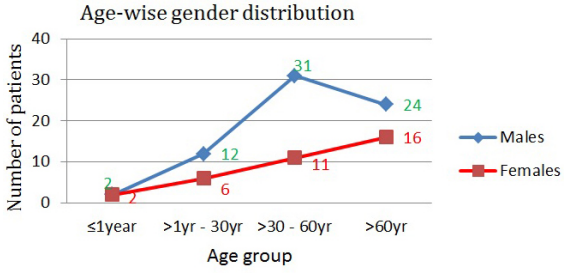

Figure 4: Age-wise gender distribution of *Candida.*

Among various samples (Figure 5) included in this study, maximum *Candida* isolates were seen in Blood (75%) followed by Pus (9%), Central line tips (4%), Pleural fluid (4%) and others (8%)

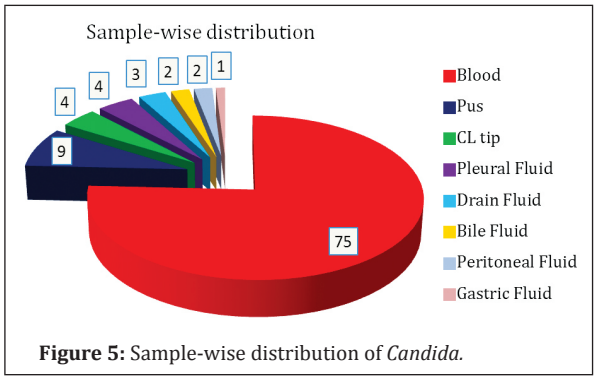

Figure 5: Sample-wise distribution of *Candida.*

Among candidemia cases, NAC (76%) were predominating; most common isolate being *Candida tropicalis (~50%).* Out of total 75 isolates of *Candida* in blood; 37(49.33%) were *C.tropicalis,* 18(24%) were *C.albicans* followed by 8(10.64%) – *C.hemulonii,* 4(5.33%) – *C.glabarata,* 3(4%) – *C.famata,* 3(4%) – *C.parapsilosis* and single isolate of each *C.auris* (1.33%) and *C.guilliermondii* (1.33%). The distribution of *Candida* spp. in blood is shown in Figure 6.

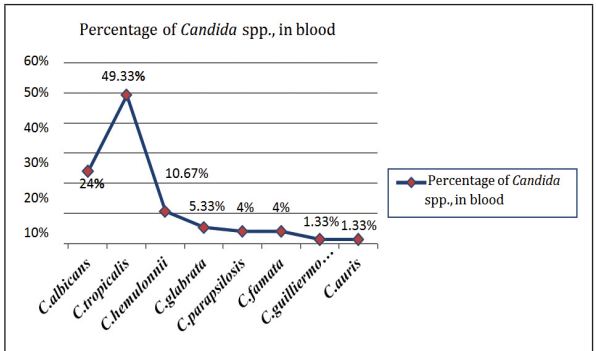

Figure 6: Graph showing distribution of various *Candida* spp., in blood.

The antifungal susceptibility among *Candida albicans* isolates for fluconazole was 80% as compared to NAC; which showed only 53.3% susceptibility (Figures 7&8). Susceptibility towards amphotericin B was relatively less in NAC (74.66%) isolates as compared with *Candida albicans* (84%) isolates.

The resistance was highest for fluconazole (46.7%) followed by AMB (25.3%) among NAC isolates. Similarly in *Candida albicans isolates*, highest resistance was seen with fluconazole (20%) followed

by AMB (16%). In this study, the susceptibility towards all the group of antifungal drugs was seen more with *Candida albicans* in comparison with NAC (Figure 9).

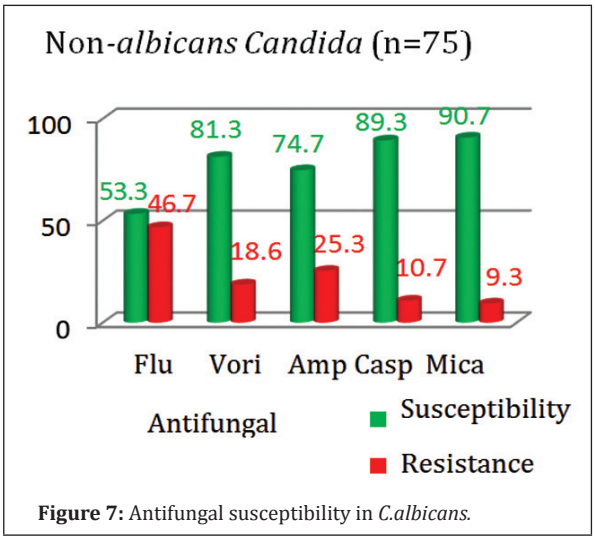

Figure 7: Antifungal susceptibility in *C.albicans.*

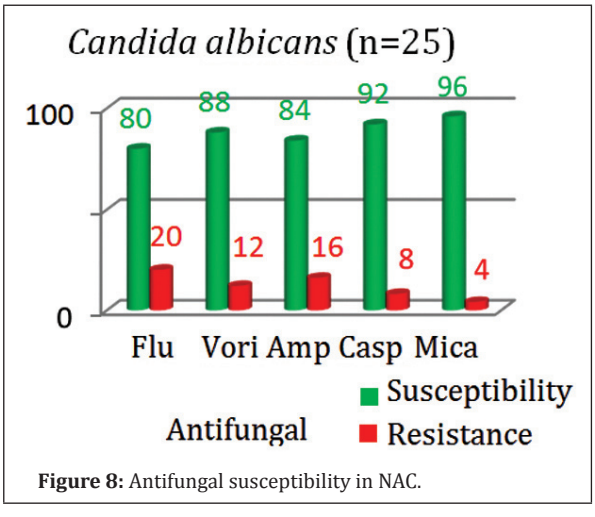

Figure 8: Antifungal susceptibility in NAC.

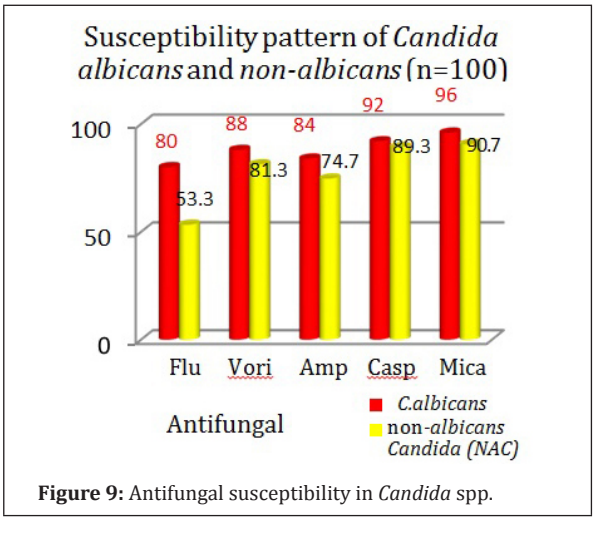

Figure 9: Antifungal susceptibility in *Candida* spp.

All the *Candida* isolates were maximally susceptible to Echinocandin group of antifungals. Among NAC species, *C.tropicalis* showed decreased susceptibility towards azoles group of antifungals. *C.famata* (4) isolates were seen sensitive to all the group of antifungals except one isolate which showed resistance to fluconazole. A special pattern was observed in all the *C.hemulonii* isolates (9). All patients with *C.hemulonii* infection showed similar pattern of antifungal susceptibility (Table 2) wherein they were all sensitive to Voriconazole, Caspofungin and Micafungin. All the 9 *C.hemulonii* isolates were resistant to fluconazole and amphotericin B. All rare NAC species (*C.hemulonii, C.auris, C.krusei, C.spherica and C.lusitaniae*) showed resistance to fluconazole whereas *C.parapsilosis* showed decreased susceptibility to polyene and echinocandin group of antifungals.

Table 2: Antifungal susceptibility pattern among *Candida* isolates.

Susceptibility of Candida isolates in percentage % (n=100)	*Flu*	*Vori*	*Amp B*	*Casp*	*Mica*
Candida tropicalis (46)	65.2	82.6	89.1	89.1	89.1
Candida albicans (25)	80	88	84	92	96
Candida hemulonii (9)	0	77	0	88	100
Candida glabrata (6)	33	66	100	100*	100
Candida famata (4)	75	100	100	100	100
Candida parapsilosis (4)	100	100	50	75	75
Candida guilliermondii (2)	50	50	50	50	50
Candida auris (1)	0	0	0	100	100
Candida krusei (1)	0	100	100	100	100
Candida spherica (1)	0	100	0	100	100
Candida lusitaniae (1)	0	100	100	100	100

**Candida glabrata* is 100% susceptible/intermediate to caspofungin based on revised guidelines [30].

Diabetes mellitus (46%) was the most common predisposing factor noticed among patients with *Candida* infection (Table 3). This was followed

by hypertension (34%), use of broad spectrum antibiotics (31%) and any recent major surgery (22%). Long duration of hospital stay (≥14days) was seen in 90% of patients with other co-morbidities and associated *Candida* infection.

There were four liver transplantation cases with candidemia. *Candida hemulonii* (50%) was the major isolate. Other two liver transplant cases had candidemia with *Candida auris* (25%) and *Candida tropicalis* (25%). Mortality among these organ transplantation patients was 75%.

Table 3: Factors associated with *Candida* Infection.

Associated factors	*No. of patients affected*
DM	46
HTN	34
Broad spectrum antibiotics	31
Major surgery	22
Carcinoma (GI and hematological malignancy)	15
Autoimmune diseases	14
CKD	11
Chemotherapy	10
Corticosteroids	9
Central line	8
CLD	8
Radiotherapy	7
Immunosuppressants	6
Liver transplantation	4

Out of total 100 patients in this study (Figure 10); 15% belonged to the pediatrics group. 20% patients out of all adults belonged to pulmonary medicine department followed by nephrology (17.64%), gastro-surgery (14.11%) and oncology (14.11%) department. Hematological and gastrointestinal malignancies formed the major part among oncology patients.

In this study, out of total 100 patients with candidiasis (Figure 11); 41 patients got treated, 28 patients with *Candida* infection and associated multiple co-morbidities expired. In drug sensitive candidiasis cases with both *C.albicans* and NAC, Tab/Inj. fluconazole was the most common drug used for treatment with duration of treatment ranging from 7-14 days. In drug resistant cases, Inj.Micafungin/Inj.Voriconazole/Inj.AMB was used depending on the susceptibility test results and patient condition. Duration of treatment ranged from 5-10 days. The outcome was favorable in cases wherein, early treatment was started.

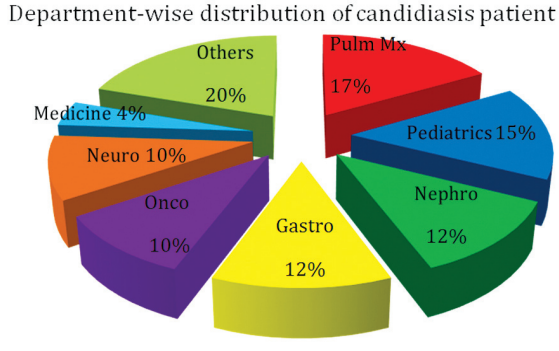

Figure 10: Graph showing department-wise distribution of candidiasis patients.

The mortality of 32.6% (Table 4) was seen in case of drug-resistant *Candida* isolates. Mortality and morbidity was higher in drug-resistant cases of *Candida* infection. In pan drug resistant cases, mortality reached up to 50%. Better outcome was seen in drug sensitive cases. But this is only relative outcome.

Table 4: Patient outcome* in *Candida* infection.

Outcome	*Treated*	*Expired*	*LAMA*	*Status unknown*
Drug-sensitive *Candida* isolates (50)	22 (44%)	11 (22%)	8 (16%)	9 (18%)
Drug-resistant *Candida* isolates [Resistant to ≥1 antifungal drug] (46)	19 (41.3%)	15 (32.6%)	4 (8.69%)	8 (17.39%)
Pan resistant *Candida* isolates (4)	-	2 (50%)	2 (50%)	-

*Includes multiple associated factors and co-morbidities in addition to *Candida* infection.

True picture of outcome is based on multiple associated factors and debilitating co-morbidities

like diabetes mellitus, underlying malignancy, major surgeries, immunosuppression, organ transplantation, chronic diseases (c/c kidney, liver or lung diseases), etc. and general conditions of patients along with *Candida* infection. Highest mortality was seen in pan-drug resistant cases. The mortality due to *Candida* infection was higher in case of infections caused by NAC (71.42%). The major attributers to this were *C.tropicalis* (42.85%) followed by *C.albicans* (28.57%) and others (*C.hemulonii*-10.7%, *C.glabrata*-7.14%, *C.auris*, *C.parapsilosis* & *C.guilliermondii*- each 3.6%).

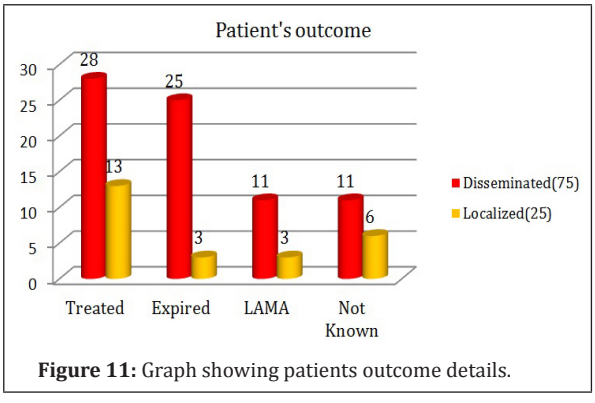

Figure 11: Graph showing patients outcome details.

Discussion

This current study details the prevalence of *Candida* infection and their antifungal susceptibility pattern in a tertiary care hospital in South India. The prevalence of *Candida* infection in this study is 1.58%, which shows comparable results with studies conducted by Gandhi et al. [31], Ahmedabad; Soumya et al. [5], Rodriguez et al. [32] in Peru.

Candida forms a part of normal human microbiota. It causes opportunistic infections in immunocompromised and debilitated patients. In this study, the predominant age group of patients affected with candidiasis belongs to the elderly group. Similar results were seen in a study conducted by Bhattacharjee et al. [33] in Kolkata and Liu et al. [34], Taiwan. In this study, only 25(25%) of the isolates were *Candida albicans* and rest 75(75%) of the isolates were NAC which shows similar trend in other studies [5, 11, 31, 32]. Whereas in contrast, *Candida albicans* formed the major isolate in studies conducted by Khan et al. [35], Amar et al. [36], Liu et al. [34] and Orasch et al. [37].

The predominant *Candida* species among NAC in present study is *Candida tropicalis* as seen with studies conducted by Bhatacharjee et al. [33] and Chakrabarty et al. [11]. In contrast, in studies conducted by Western countries; *Candida glabrata* and *Candida parapsilosis* formed the predominant NAC species [32, 37-39].

One NAC isolate was *Candida auris* in the present study which was multi-drug (MDR) resistant. It was isolated from both blood and bronchial wash of a liver transplantation patient. On repeated test by Vitek 2 compact, this organism was misidentified as *Candida famata* twice. As this organism is put on high alert by CDC owing to its high mortality and MDR nature leading to difficult treatment; we confirmed the identity of the organism by sending it to reference laboratory at Mycology department, PGIMER, Chandigarh. Confirmation was done there using MALDI TOF automated system. Eventually even with effective parenteral treatment due to disseminated infection and immunocompromised state, the patient succumbed to death [40-42].

In the present study, gender predominance of Candidiasis infection was seen in males (67%) as seen in other studies [31-33]. Among various samples included in this study, maximum *Candida* isolates were seen in blood (75%) showing disseminated infection is common with *Candida* in susceptible individuals. Hence, early identification and prompt treatment based on the *Candida* speciation and its antifungal susceptibility is of utmost importance. Similar results were substantiated in various other studies conducted by Khan et al. [35], Jaggi et al. [10] and Dharwad et al. [43].

The antifungal susceptibility in present study for fluconazole among *Candida albicans* isolates was higher as compared to NAC. Study by Bhatacharjee et al. [33] shows similar results. This shows the importance of maintaining the rational use of antifungals. The choice of antifungal drug depends on various factors like local epidemiology and the patient's co-morbidities.

The emergence of NAC spp. has initiated the need of antifungal susceptibility testing of *Candida* isolates. The NAC species are comparatively less susceptible to fluconazole and amphotericin B [28, 33]. *Candida krusei* shows intrinsic resistance to fluconazole [5, 44]. This was justified in present study. All rare NAC species (*Candida hemulonii, Candida auris, Candida krusei, Candida spherica and Candida lusitaniae*)

showed higher resistance to fluconazole. *Candida albicans* and *Candida tropicalis* showed 16% and 10.8% resistance to Amphotericin B, respectively in this study. Studies conducted by Nazir et al. [45], Sandhu et al. [46] and international studies by Jamil et al. [47] and Badiee et al. [48] shows similar results. In another study conducted by Bhattacharjee et al. [33], further high resistance was seen in *Candida albicans* and *Candida tropicalis* against amphotericin B. In contrast, various other studies shows very low or nil resistance to amphotericin B [5, 28, 32, 43, 49-50]. Many studies show amphotericin B testing as not applicable. This is because detection of resistance to amphotericin B by the CLSI M27-A2 BMD method has been problematic due to the very narrow range of MICs obtained [51-53]. This implies that further research and studies are needed to standardize polyene testing for yeasts. *C.parapsilosis* showed decreased susceptibility to polyene and echinocandin group of antifungals. Maximum susceptibility towards all the antifungal groups was seen by *Candida famata* in this study. Novel finding in present study was that among *Candida hemulonii* isolates (9); all patients with *Candida hemulonii* infection showed similar pattern of antifungal susceptibility. They were all sensitive to Voriconazole, Caspofungin and Micafungin but all 9 *Candida hemulonii* isolates were resistant to fluconazole and amphotericin B. This could be indicative of evolving intrinsic resistance to FLU and AMB but this information needs further research owing to limited number of isolates to come to any conclusion.

Azole drugs still remain a safe and effective choice for treatment for mild to moderate *Candida* infection, as it is available in both parenteral and oral formulations with high bioavailability. Irrational use of fluconazole for prophylaxis and treatment and prolonged duration or incomplete treatment could be the reasons of present emergence of high drug resistance to fluconazole.

The availability of new fungal markers, such as beta-d-glucan, has opened the door to research in early therapy strategies such as empirical therapy in high risk hosts. But they are still under process of being standardized and needs more studies like this to support and direct in the empiric treatment of high-risk hosts.

In this study, the NAC shows better susceptibility to Echinocandin group of drugs also seen in other studies [5, 11]. Patients who showed resistance to fluconazole and amphotericin B were treated with Echinocandin group of drugs; in most cases with Inj.Micafungin. Echinocandins are highly expensive and cannot be afforded by a majority of the Indian population. Hence, prevention of infection by improving the living status, nutrition and maintaining strict infection control in ICU's and wards in hospitals should be given higher importance.

Strength of the study

This is a prospective study and the sample size was calculated statistically. The samples like oral and vaginal swabs, urine, sputum, endotracheal secretion and bronchial wash were excluded from the study. Samples like blood, deep pus, fluids and tissues representing invasive and disseminated candidiasis were only included in this study. The final species identification and antifungal susceptibility testing was done by automated Vitek 2 compact system. This avoided manual errors of interpretations and those isolates with good identification were only included in the study.

Limitations of the study

Molecular methods and sequencing could not be done due to economic constraints. LAMA patients could not be followed up; hence the outcome could not be measured in those cases. This study has a limitation of a single institutions experience. Group of population are limited; hence generalizability of these findings to the settings with different patient populations is the limitation of this study. Amphotericin B resistant isolates were not checked using microbroth dilution method which is gold standard method.

Future directions

Further studies assessing the predisposing factors, species level identification and involving larger group of population affected with candidiasis are recommended. Regular surveillance of local antifungal susceptibility patterns and formulation of empiric treatment guidelines for high risk patients is suggested.

Conclusion

There is a significant epidemiological shift in

candidiasis cases due to NAC species. This is due to the advanced treatment and diagnostic interventions. *Candida tropicalis* is the most frequent pathogen isolated in our tertiary care center. *Candida albicans* and NAC both shows reduced susceptibility to azoles mainly fluconazole; but NAC shows higher decrease in susceptibility pattern towards azoles. *Candida albicans* still shows good susceptibility towards polyene group and echinocandins. NAC shows decreased susceptibility to polyene as compared to *C.albicans.* Echinocandins forms better empirical choice in invasive NAC infections but choice of azoles or echinocandins differs based on severity of infection and individual patient condition. Based on the present results and trends, it becomes essential to routinely identify *Candida* isolates at species level, and detect evolving resistant strains by antifungal susceptibility test. Furthermore, there is a continued need for surveillance to monitor changes in the epidemiological features and antifungal susceptibility and also to develop and evaluate prevention strategies

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Conflict of interest

Authors declare no conflict of interest.

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