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Emerging Role of Non Albican Candida in Systemic Candidiasis

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A B S T R A C T

Systemic candidiasis (SC) is an important fungal infection in which new candida species are emerging with their high resistance to routine antifungals. In this study out of 270 candida isolates, *Candida albicans* and *Candida tropicalis* are the most common isolated species but also highlightened the role of new emerging candida species like *C.krusei, C.glabrata, C. dublinensis* which have also shown high resistance rates to common antifungals used in routine. Thus, this short communication will be very useful in evaluating the role of evolving Candida species in this new world.

Introduction

Systemic candidiasis (SC) is the most common invasive fungal infection as the nosocomial infection in patients undergoing major surgeries during prolonged neutropenia, transplantation and extended hospital stays of days to weeks,. This infection is potentially a life-threatening complication in immunocompromised patients. The introduction of novel antineoplastic agents, antifungals, antibacterial and antivirals over the past 10 years has led to a shift in fungal epidemiology and development of resistance among *Candida* strains. Antifungal resistance surveillance serves as a major strategy for prophylaxis, empirical therapy, and treatment of SC. For the management of patients suffering from SC, determination of the changes in the distribution of *Candida* species and respective resistance pattern to antifungal agents are important (Hughes *et al*., 2002 and Badiee *et al*., 2011)

The aim of present study is to identify the hanging spectrum of Candida species in clinical infections and to evaluate the role of emerging non albicans Candida in systemic candidiasis by analyzing their resistance pattern to available antifungal drugs.

Materials and Methods

All the 270 isolates of candida obtained from different clinical specimens during the year 2010-2014were speciated using both conventional and automated techniques.

Conventional identification was performed by observing the morphology on the Corn Meal Agar, with color development on the Triphenyl Tetrazolium Chloride Agar, the CHROM agar (BD, Franklin Lakes, New Jersey, USA), and germ tube tests. The VITEK 2 YST ID colorometric card was used for automated identification. Antifungal susceptibility was performed using the VITEK 2 system (bioMerieux Pvt. Ltd., St. Vulbas, France). The following antifungal drugs were tested: Amphotericin-B, Fluconazole, Flucytosine, and Voriconazole. The conventional method of identification was taken as our gold standard in cases of discordance in the identification of *Candida* spp. by the automated VITEK 2 system and the conventional methods.

Results and Discussion

The most common sites of the isolation of candida species were blood and urine followed by endotracheal aspirate, sputum, high vaginal swab, central line, pus, oral swab and cerebrospinal fluid. Among the isolated candida, nonalbican candida(60%) outnumber the *Candida albicans*(38%). The most common species isolated from the patients was *C. albicans(38.85%)*followed by *C.tropicalis* (30%).Also *C. glabrata*, C. *krusei* and *C. dublinensis* emerged as an important candida species which accounts for 20% of total isolates. Other candida species were 10% of total isolates (Table 1).

Resistance rates for amphotericin B(A MB), Fluconazole (FLU), Flucytosine (FCy), itraconazole (ITR), Voriconazole (VOR) were 3.7%, 13%,.75%, 5% and 5% respectively. Fluconazole showed highest resistance rate for bothalbicans as well as non albican Candida. It has been seen that non-albicans Candida were more resistant to all the drugs as compared to *C.albicans.* Among the most common emerging Non albicans Candida mentioned in our study *C.krusei* was the most resistant species (16/16) followed by *C.glabrata* (8/26), *C.tropicalis* (6/82)and *C.dublinensis* (2/12)for the drugs tested.All the strains of *C.krusei* were found resistant to Fluconazole (Table 2)

Resistance rates seen in our study is quite consistent with the study done by pahwa *et al.,* with amphotericin B (AMB), Fluconazole (FLU), Flucytosine (FCy), itraconazole (ITR), Voriconazole (VOR) showing resistance rate of 2.9%, 5.9%, 0.0%, 4.2% and 2.5% respectively. Also, all the strains of *C.krusei* were found resistant to fluconazole. High level of resistance for nonalbicans in comparison to candida albicans has been seen in many other studies done so far (Pahwa *et al.,* 2014)

The distribution of the species are different in various regions and studies. A study by badie *et al* showed *C.krusei* and *C.glabrata* as the commonest nonalbicans followed by *C.kefyr, C.parapsilosis*(2)Vaghela *et al* reported *C.glabrata*(26%) followed by *C.tropicalis* (18.5%),*C.parapsilosis*(15%), *C.gullermondi*(7%) (Vaghela *et al.,* 2015).

During recent decades, several countries around the world have witnessed a change in the epidemiology of *Candida* infections, characterized by a progressive shift from a predominance of *Candida albicans* to new emerging non-*albicans Candida* species (including *C. glabrata*and *C. krusei*). These non- *albicans Candida* species (e.g., *C. glabrata* and *C. krusei*) exhibit resistance to traditional triazole antifungals like fluconazole, and may also demonstrate cross-resistance to newer triazoles (Oberoi *et al*., 2012)

Table.1 Distribution of Candida species in different clinical isolates

	Blood	**Urine**	**Sputum**	**Endo tracheal aspirate**	**Central line**	**HVS**	**Pus**	**Oral swab**	**CSF**	**Total**
Candida albicans	46	22	08	18	07	02	00	00	02	105
Candida tropicalis	24	30	09	06	04	05	02	00	02	82
Candida glabrata	04	10	03	02	02	04	01	00	00	26
Candida krusei	08	01	01	04	01	01	00	00	00	16
Candida dublinensis	00	00	03	00	00	04	02	03	00	12
Candida sake	02	02	00	01	01	02	00	01	00	09
Candida intermedia	01	01	01	01	01	01	01	00	00	07
Candida sphaerica	01	01	01	00	00	01	00	01	00	05
Candida globosa	00	01	00	00	00	01	00	00	00	02
Candida famata	01	01	00	00	00	00	00	00	00	02
Candida rugosa	00	01	00	00	00	01	00	00	00	02
Candida gullermondii	00	01	00	00	00	00	00	01	00	02
Total	87	71	26	32	16	22	06	06	04	270

Table.2 Showing number of Candida isolates resistant to antifungal agents.

	C.albicans (n=105)	*C.tropicalis* (n=82)	*C.glabrata* (n=26)	*C.krusei* (n=16)	*C.dublinensis* (n=12)	Other (n=29)	Total (n=270)
Anti Fungal tested.							
Amphotericin B	01	02	02	04	00	01	10(3.7%)
Fluconazole	03	06	08	16	02	00	35 (13%)
Itraconzole	01	03	03	04	01	02	14(5%)
Variconazole	01	02	02	04	01	03	13(5%)
flurocytosine	00	01	00	01	00	00	02(.75%)

In our study, although *C.tropicalis* (30%) is the most common non albican candida but the role of these new emerging candida species (*C.krusei*,10%; *C.glabrata*,6%) cannot be unseen. A remarkable point in our study is emergence of *Candida dubliniensis (*4%) which were isolated from high vaginal swab, sputum, oral swab and pus and showed high azole resistance in comparison to other nonalbican candida.

Candida dubliniensis is an opportunistic yeast that has been implicated in oropharyngeal candidiasis and vulvovaginal candidiasis and were found in many studies in patients infected with Human Immunodeficiency Virus (HIV). They are under-reported due to their similarity with *Candida albicans*. Further antifungal susceptibility test showed higher resistance among *C. dubliniensis* isolates to azoles

compared to *C. albicans* (Chunchanur *et al*., 2009 and Theill *et al.,* 2016)

Thus the role upcoming nonalbicans candida in this new world cannot be neglected as they also showed high level of resistance to commonly used azole drugs.

Based on the above results it is clear that the importance of monitoring changes in the distribution of pathogenic *Candida* species, their virulence property and their resistance rates is essential for successful treatment of systemic candidiasis.

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