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Emergence of Non Albicans *Candida* in a Tertiary Care Hospital, Uttarakhand

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Abstract : *The incidence of Candida infection is increasing globally. The normal microbial flora of human being give rise to life threatening endogenous infections in immunocompromised patients and also associated with the hospital acquired infection. Due to the advancement in the medical field and overuse of broad spectrum antibiotics, non albicans Candida (NAC) became the chief pathogenic organism over Candida albicans. The aim of the present study was to encounter different species of NAC and their antifungal susceptibility. Hundred and eighty different clinical isolates of Candida species were subjected to identification and antifungal test in a tertiary care hospital. The standard conventional yeast identification system was followed. NAC found higher in number over Candida albicans. C. tropicalis which showed predominance among NAC and also have shown highest resistance against azole group of drugs. Although C. albicans and other Candia species are normal microbiota of skin and mucous membrane but colonization of these organisms may lead to life threatening infections in hospitalized or critical care patients. It is therefore suggested that routine culture system need to be put for identification along with antifungal susceptibility test for yeast as well.*

Keywords: *Antifungal susceptibility Candida spp, non albicans Candida*.

I. Introduction

Invasive fungal infections are increasing since over the past decades largely because of increasing size of population at risk [1]. It is now an emerging problem of significant magnitude in hospitals during last two decade, especially in the ICUs, which are epicenter for infections such as candidemia and invasive *Candida* infection [2]. *Candida* infections increased due to increasing number of patients receiving chemotherapy and other immunosuppressive therapies, innovations in transplantation surgery, use of broad-spectrum antibiotics, higher number of patients hospitalized in the intensive care units and invasive procedures performed [3]. Non albicans species of *Candida* are currently the pathogens most frequently recovered from adults and children in tertiary care medical centers [4]. Epidemiological data from the Indian subcontinent showed that 67-90% nososcomial Candidemia were due to non albicans species of *Candida* [5,6]. Epidemiological studies have revealed emergence of species that may vary geographically in frequency of isolation. It is essential for laboratory to identify clinical isolates of *Candida* to the species level and consider in vitro susceptibility testing which will aid in therapeutic decision making of that clinical set up [7].

II. Materials And Methods

A total of 180 *Candida* species isolated from April-January 2013 in the Central Microbiology laboratory of tertiary care hospital were included in the study. The *Candida* species were isolated from different clinical samples received from outdoor and indoor departments (ICUs, medicine, surgery, paediatrics, obstetrics and gynecology). Due permission was taken from concerned authority and patients detail was recorded. Repeat samples were taken whenever colonization was suspected. Culture positive yeasts were subjected to species level identification in the mycology section of Department of Microbiology. Blood cultures bottles were incubated in BacTAlert3D (Biomerieux, France) automated blood culture system, where positive bottles were confirmed by gram stain and sub cultured on blood, MacConkeys agar and Sabouraud dextrose agar. For identification of yeast, standard identification protocol was followed [8,9]. Germ tube test was done with 0.5 ml of pooled human serum. Dalmau plate culture for chlamydospore was done on corn meal agar (CMA) with 1% Tween 80 and the plate was studied after 3-5 days of incubation at 27˚C. Isolates were also cultured on CHROM agar (HiMedia, Mumbai, India) plates and identified on the basis of color of the colonies. Confirmation of species was done on the basis of sugar fermentation and assimilation tests. Antifungal susceptibility test was done by Kirby-Bauer disc diffusion method on MHA agar supplemented with 2% glucose and 0.5µg/ml methylene blue dye. Readymade antifungal disc (HiMedia, Mumbai, India) of AmphotericinB (20mcg), Fluconazole (10mcg), Itraconazole (10mcg), Ketoconazole (30 mcg) and Voriconazole (1mcg) were used for antifungal susceptibility test.

III. Result

Candida isolates obtained from different samples (Fig.1A) received from different departments (Fig.1B) were included in the study. In this study out of 180 *Candida* isolates, NAC found higher in number 152 (84%) and *Candida albicans* 28 (16%)(Table.1). The occurrence of *C. albicans* and NAC in different ages of both sexes is given in Table.2. Various co-morbid factors which were found to be associated with *Candida* infection are listed in (Table.3). The results were analyzed using simple statistical test (χ^2-test).

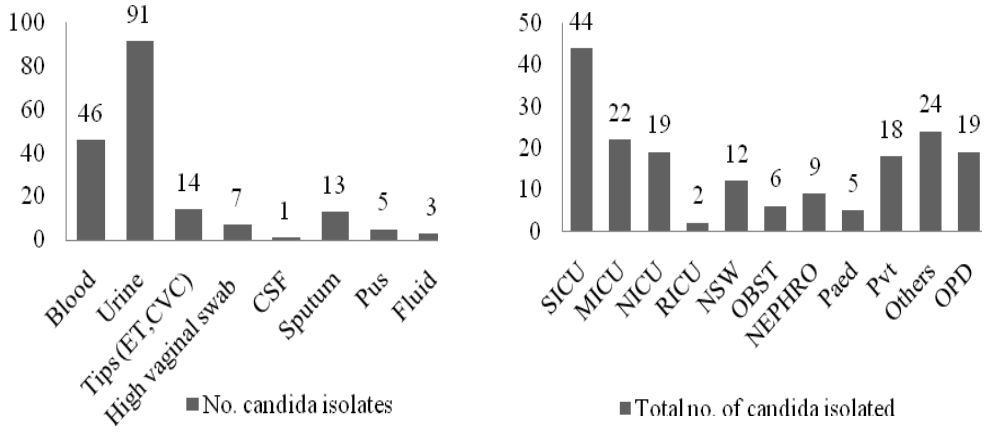

FIGURE. 1: A. Distribution of *Candida* isolates in different clinical samples. B. Distribution of *Candida* positive in IPD and OPD.

TABLE. 1: Distribution of different *Candida* species in patient population

Isolates	**Number**	**%**
C. albicans	28	(15.6%)
Non albicans *Candida* (n=152)		
C.tropicalis	104	(57.8%)
C.glabrata	8	(4.4%)
C.krusei	10	(5.6%)
C.kefyr	15	(8.3%)
C.zeylanoides	9	(5%)
C.dubliniensis	4	(2.2%)
C.haemulonii	2	(1.1%)
Total	180	100%

TABLE. 2: Distribution of positive samples among different age groups and sex of patient

Age in years	***C. albicans* (n=28)**		**Non-*albicans Candida* (n=152)**	
	Male	Female	Male	Female
0-10	2	0	19	8
11-20	0	1	1	6
21-30	2	4	10	13
31-40	2	0	3	4
41-50	2	1	16	5
51-60	2	0	11	5
>60	7	5	38	13
Total	**17**	**11**	**98**	**54**

TABLE. 3: Various co-morbid factors associated with patient in study

Co-morbid factor	**Total no./180**	**Co-morbid factor**	**Total no./180**
Indwelling urinary catheter	110	Preterm delivery	8
Long term Antibiotic therapy	94	Low birth weight	6
Surgery	52	VP shunt	6
IV line	49	Septicemia	5
Ventilator	28	Antitubercular therapy	4
Blood transfusion	25	Hypothyroidism	3
CVC	21	Septic meningitis	3
Pregnancy	14	Dyspnoea	1
T_2DM	14	Acute kidney infection	1
Chronic kidney disease	10		

CVC-

Central vascular catheter, T_2DM-Type 2 diabetes mellitus

IV. Discussion

Infections with NAC are numerically dominant over those caused by *C. albicans*. By using $\chi 2$ test, the difference between *C.albicans* and NAC was found highly significant ($p<0.0001$). This study observed the predominant isolate in all samples is *C. tropicalis* followed by *C. albicans*. Various Indian studies also showed *C. tropicalis* as a predominant organism [10,11,12]. The emergence of species other than *C. albicans* is the selection of less susceptible species by the pressure of antifungal agents such as fluconazole [13]. After extensive literature survey it has been found that resistance to fluconazole has increased. [5,14] There may be several factors responsible for resistance in deferent clinical conditions including wide spread or consistent use of fluconazole. Resistance against fluconazole found highest with *C. tropicalis* (29%) and also showed highest azole resistance as compared to other species. Among all the one hundred eighty isolates of *Candida*, 71(39.4%) showed resistance to fluconazole, which is again highest number among the all antibiotics used. The decreased susceptibility against fluconazole is a matter of concern because fluconazole still is drug of choice of empiric antifungal therapy. *C. krusei* is known for its innate resistance to fluconazole, [15] our study showed 70% resistance. This actually creates problem when species level identification is not done, which may lead to treatment failure. Among the azoles voriconazole was more sensitive than the other azoles and the difference was singnificant ($p<0.0001$). Due to its broad spectrum activity, voriconazole can be preferred for those species of *Candida* which are intrinsically resistant to fluconazole [8].

The susceptibility pattern of all *Candida* isolates showed 87% sensitivity to amphotericinB; except one resistant *C. kefyr*, all isolates showed zero resistance (Table.4) and 13% were sensitive dose dependent. Other Indian studies showed 91-92% sensitivity in comparison to our study [10,11]. As compared to azoles, amphotericinB found more sensitive ($p<0.0001$).

Candida in urine is a therapeutic challenge because presence of it represents many conditions which require interpretation. *Candida* species use several intrinsic adherence mechanisms to initially colonize and invade uroepithelium of both the upper and lower urinary tract. Yeast in urine is associated with increased mortality especially in ICU patients with several comorbid factors, nevertheless, candiduria may be a marker for serious underlying illness [16]. No studies have unequivocally established the importance of pyuria or quantitave urine cultures for UTI due to *Candida* [17].

Most of the risk factors shown in Table 3 represent common interventions or condition in the hospitalized ICU settings. It is unclear whether they have a causal relationship to the disease or are just associated markers indicating severity of illness and other predisposing conditions [18].

V. Conclusion

The change of pattern in the species distribution of *Candida* is variable in different geographical area which has made the species level identification compulsory along with antifungal susceptibility test. Periodic surveillance of new species and the antifungal sensitivity test can serve as a template for development of local guideline for the critical care patients. The colonizing *Candida* species can't be overlooked and rather need to be correlated with the critical patient conditions.

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References

[1] Warnock D W. Trends in the Epidemiology of invasive Fungal infections. Jpn. J. Med. Mycol, 2007; 48:1-12.
[2] Kaur R, Goyal R, Dhakand MS, Bhalla P, Kumar Rakesh. Epidemiology and virulence determinants including Biofilm profile of Candida infections in an ICU in a tertiary Hospital in India. J of Mycology, 2014; ID: 303491, 1-8.
[3] Baran N, Salman I S, Yurtsever1 S G, Ozdemir R, Gungor S, Yurtsever S and Demirci M. Typing of Candida species isolated from blood cultures and analysis of their in vitro antifungal susceptibilities. African J of Microbiol Research, 7(41),2013, 4882-4885.
[4] Pappas P G, John H R, Jeannette L, Richard JH, Larsen RA, Powderly W, Kauffman CA, Hyslop N, Mangino JE, Champman S, Horowitz HW, Edwards JE and Dismukes WE. A prospective Observational Study of Candidemia: Epidemiology, Therapy, and Influences on Mortality in Hospitalized Adult and Pediatric patients. Clinical Infect Dis 37, 2003, 634-43.
[5] Kothavade R J, Kura MM, Yaland AG and Panthaki MH. Candida tropicalis: its prevalence, pathogenicity and increasing to fluconazole. J Med Microbiol, 59, 2010, 873-80.
[6] Kothari A and Sagar V. Epidemiology of Candida bloodstream infections in a tertiary care institute in India. Indian J Med Microbiol, 27, 2009, 171-2.
[7] Pfaller MA and Diekema D J. Epidemiology of Invasive Candidiasis: A Persistent Public Health problem. Clin. Microbiol. Rev 20(1), 2007, 133-163.
[8] Candidiasis in Chander J (3rd ed), A Textbook of Medical Mycology (New Delhi: Mehta Publisher, 2009) 212-30.
[9] Yeast and Yeast like Organism in Laron DH. (5th ed), Medically important Fungi; A Guide to Identification (USA: ASM press, 2011) 117-168.

[10] Pahwa N, Kumar R, Nirkhiwale S, Bandi A. Species distribution and drug susceptibility of Candida in clinical isolates from a tertiary care center at Indore. Indian J Med Microbiol, 32(1),2014,44-48.
[11] Adhikary R, S Joshi. Species distribution and antifungal susceptibility of candidemia at a multisuperspeciality center in southern India .Indian J Med Microbial ,29(3),2011, 309-311.
[12] Saha R, Shukla Das Das. Pattern of Candida isolates in Hospitalized Childern. Indian J Pediatrics, 5, 2008, 858-860.
[13] Pfaller MA. Nosocomial Candidiasis: Emerging Species, Reservoirs, and mode of transmission. Clinical Infect Dis 22,1996,89-94.
[14] Giri S, Kindo A J, A review of Candida species causing blood stream infection. Indian J Med Microbiol, 30(3), 2012, 270-8.
[15] Narain S. Neonatal systemic candidiasis in a tertiary care centre. Indian J of Med Microbiol, 21(1), 2003, 56-58.
[16] Fisher J. F. Candida urinary tract infection-epidemiology, pathogenesis, diagnosis and treatment: Executive summary. Clin Infect Dis 52(6), 2011, 429-432.
[17] Kauffman CA. Candiduria. Clinical Infect Dis,41(6), 2005, 371-376.
[18] Pfaller MA, Diekema DJ, Colombo AL, Kibbler C, Ng KP, Gibbs DL, et al. Candida rugosa, an emerging fungal pathogen with resistance to azoles: geographic and temporal trends from the ARTEMIS disk antifungal surveillance program. J Clin Microbiol 44(10), 2006, 3578-82.

Table. 4: Antifungal susceptibility pattern of *Candida* species

Amphotericin B									
Resistant	0(0%)	0(0%)	0(0%)	0(0%)	1(6.67%)	0(0%)	0(0%)	0(0%)	1(0.5%)
SDD	6(21.4%)	11(10.6%)	3(37.5%)	0(0%)	1(6.67%)	2(22.2%)	0(0%)	0(0%)	23(12.8%)
Sensitive	22(78.6%)	93(89.4%)	5(62.5%)	10(100%)	13(86.6%)	7(77.8%)	4 (100%)	2(100%)	156(86.7%)
Total	28	104	8	10	15	9	4	2	180(100%)
Itriconazole									
Resistant	5(17.9%)	20(19.2%)	6(75%)	2(20%)	2(13.3%)	0(0%)	2(50%)	0(0%)	37(20.6%)
SDD	12(42.9%)	46(44.2%)	2(25%)	4(40%)	6(40%)	3(33.3%)	0(0%)	1(50%)	74(41.1%)
Sensitive	11(39.2%)	38(36.6%)	0(0%)	4(40%)	7(46.7%)	6(66.7%)	2(50%)	1(50%)	69(38.3%)
Total	28	104	8	10	15	9	4	2	180(100%)
Ketoconazole									
Resistant	10(35.8%)	29(27.9%)	6(75%)	3(30%)	4(26.7%)	1(11.2%)	4(100%)	0(0%)	57(31.6%)
SDD	11(39.2%)	31(29.8%)	2(25%)	2(20%)	2(13.3%)	4(44.4%)	0(0%)	0(0%)	52(28.8%)
Sensitive	7(25%)	44(42.3%)	0(0%)	5(50%)	9(60%)	4(44.4%)	0(0%)	2(100%)	71(39.4%)
Total	28	104	8	10	15	9	4	2	180(100%)
Fluconazole									
Resistant	11(39.2%)	30(28.9%)	6(75%)	7(70%)	8(53.3%)	6(66.7%)	2(50%)	1(50%)	71(39.4%)
SDD	6(214%)	7(6.8%)	1(12.5%)	2(20%)	2(13.3%)	1(11.1%)	1(25%)	0(0%)	20 (11.1%)
Sensitive	11(39.2%)	67(64.4%)	1(12.5%)	1(10%)	5(33.3%)	2(22.2%)	1(25%0	1(50%)	89(49.4%)
Total	28	104	8	10	15	9	4	2	180 (100%)
Voriconazole									
Resistant	9(32.1%)	25(24.0%)	1(12.5%)	0(0%)	3(20%)	1(12.5%)	0(0%)	0(0%)	39(21.7%)
SDD	0(0%)	8(7.6%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	8 (4.4%)
Sensitive	19(67.9%)	71(68.2%)	7(87.5%)	10(100%)	12(80%)	8(88.9%)	4(100%)	2(100%)	133(73.9%)
Total	28	104	8	10	15	9	4	2	180(100%)