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Candiduria: current scenario

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Abstract : *Candida is a commensal of urogenital tract. With the indiscriminate use of antibiotics and wider spectrum of immunocompromised states Candida is gaining importance as pathogenic fungi. The present study was conducted with the aim of assessing the true prevalence of candiduria in our settings as well as analysing their antifungal resistance pattern. This study was conducted over a period of 6 months from July to December 2012. Identification of Candida species and the antifungal susceptibility was performed manually. The results obtained were analysed statistically using chi-square test for significance. A total of 1072 culture positive urine samples were reported during this period of which 132/1072(12.3%) urine samples showed growth of yeast cells. On speciation 25/132 (18.9%) were found to be C. albicans while 111/132 (84.1%) were identified as non albicans Candida, which included C.tropicalis, C.glabrata, C.kefyr and C.krusei. C.albicans showed resistance to almost all the antifungal drugs tested in variable proportions. Candida earlier assumed as nonpathogenic has acquired a greater clinical role in today's scenario of increasing risk factors, emerging antifungal resistance and immunocompromised states. Though caution has to be maintained in reporting candida from urine but it is suggested not to ignore Candiduria, since it may even be a marker of disseminated candidiasis.*

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Keywords: Antifungal susceptibility, Candiduria, *C.albicans,* non albicans candida,

I. INTRODUCTION

The most common yeasts that infect humans are the *Candida* species and *Cryptococcus* species[1]. The genus *Candida* includes about 150 different species, but only a few are known to cause human infections. More than 90% of yeast infections due to *Candida* are attributed to the species- *C. albicans, C. glabrata, C. parapsilosis, C. tropicalis* and *C. krusei*. Others are *C. lusitaniae* and *C. dubliniensis* [2] .

The unrestricted use of antibiotics can induce infections with *C. albicans* by causing its overgrowth. Pathogenic fungi of the *Candida* genus are among the main causes of hospital-acquired infections [3,4] . Over the period 1980–1990, hospital data reported a steady increase in the rate of nosocomial fungal infections including *C.albicans* infections from 2.0 to 3.8 per 1000 discharges. The increase is likely multi-factorial, including changes in clinical practice such as increased use of long term venous catheters, use of broad-spectrum antibacterial agents and improved laboratory techniques for identification of unusual *Candida* species [5,6].

The presence of *Candida* in urine is referred to as candiduria. The majority of patients with candiduria suffer a completely benign process [7]. Urinary candidiasis is one of the most confusing forms of candidiasis since the differentiation between colonization and real infection is difficult to make. Isolation of *C. albicans* in urine is believed to represent colonization or contamination. Candiduria can also be a sign of candidemia or invasive renal candidiasis. It can cause candidemia during invasive urologic procedures [8,9].

Distinguishing contamination from true infection is not easy despite existence of reliable diagnostic criteria for significant candiduria. Several predisposing factors such as use of indwelling urinary devices, diabetes mellitus, antibiotic use, immunosuppressive therapy, extremes of ages and female sex have been identified as being associated with increase of *Candida* growth in urine [10]. Human infections by *Candida* species are usually endogenous. *Candida* can be acquired from exogenous sources through the contaminated hands of health care workers, contaminated infusates and biomaterials [11].

Antifungal agents commonly used in treating yeasts infections of the urinary tract are fluconazole and amphotericin B. Differences in antifungal susceptibilities have been reported in different countries [12].

II. MATERIAL & METHODS

The study was conducted over a period of six months from July to December 2012 in a tertiary care hospital at Dehradun, Uttarakhand.

2.1 Inclusion criteria

The urine samples submitted to the laboratory showing pure growth of yeast cells on repeat sampling, a significant colony count with $>10^4$ colony forming units/ml and direct microscopy collaborating that candiduria was present by evidence of pyuria and yeast cells were included in this study .

Detailed information regarding probable risk factors like age, sex, pregnancy, diabetes mellitus, use of broad spectrum antibiotics, indwelling urinary tract catheter and presence of central venous line were recorded and included in this study.

2.2 Exclusion criteria

Urine samples which failed to grow yeast cells on repeat samples were considered contaminants and excluded from this study.In the laboratory, the urine sample was processed as for bacterial culture. The loopful of urine sediment was applied to a small area of the sabouraud's dextrose agar (Oxoid, UK) plate to make a pool. The inoculating loop was then used to spread the inoculum from the pool. A wet film was prepared and examined under the microscope for pus cells and yeast cells. Growth obtained were further identified and characterized using standard techniques on the basis of Gram staining, Reynold's Braude phenomenon, Culture on CHROM agar, chlamydospore formation on corn meal agar, sugar fermentation and sugar assimilation test. Following which antifungal drug susceptibility was performed using Kirby Bauer's disc diffusion method using commercially available discs on Muller Hinton Agar with 2% glucose. Results thus collected were analysed statistically using chi-square test for the relevance of this study.

III. RESULT

A total of 1072 culture positive urine samples were reported from the urine samples submitted for aerobic culture. Out of which 132/1072(12.3%) urine samples showed growth of yeast cells. Growth of *C. albicans* was observed in 25/132(18.9%), while111/132(84.1%) were identified as non albicans *Candida*. This difference was found to be statistically significant ($p<0.0001$). It was found that *C. tropicalis* was the predominant yeast isolated 90/132 (68.2%). Other *Candida* species identified are shown in Table 1. With 56.8% males and 43.2% females, a male preponderance was observed in our study. Maximum *Candida* isolates were observed in the age groups from 21 to 70yrs. Table 2 shows that of the *C. albicans* 8/25(32%) were isolated from Surgical ICU and of the non albicans *Candida* predominant isolation was from Obstretics and Gynaecology ward, 30/107 (28%). When risk factors associated with candiduria were observed, we found that catheterization 97/387 (25%) and antibiotic therapy 23.8% (92/387) were the most common risk factors leading to UTI due to *Candida* infection (Table 3).

The isolates showed variable susceptibility to the antifungal drugs. When susceptibility of Amphotercin B and azoles were compared and analysed it was found to be statistically significant ($p<0.001$) (Table 4).

TABLE 1: Species wise distribution of isolates

Isolates	Number
Candida albicans	25
Candida tropicalis	90
Candida kefyr	10
Candida krusei	5
Candida glabrata	2
Total	**132**

Table 2: Ward wise distribution of *Candida* isolates

WARD	*C. albicans* (n=25)	*C. tropicalis* (n=90)	*C. kefyr* (n=10)	*C. krusei* (n=5)	*C. glabrata* (n=2)
Medicine ward	2	19	0	1	0
Surgery ward	2	11	1	0	0
Neurosurgery ward	1	4	0	0	0
Nephrology ward	4	7	0	0	0
Obs/Gynae ward	3	22	4	3	1
Paediatric ward	0	2	0	0	0
Medicine ICU	5	17	1	1	0
Paediatric ICU	0	2	0	0	0
Surgical ICU	8	6	4	0	1

Table 3: Risk factors and association of *Candida* isolates

Risk factor	Number of cases
Male	75
Female	57
Antibiotic therapy	92
Catheterised	97
Diabetes mellitus	17
CVC	26
Pregnancy	22
ATT	1

CVC-central venous catheter, ATT-anti tubercular treatment

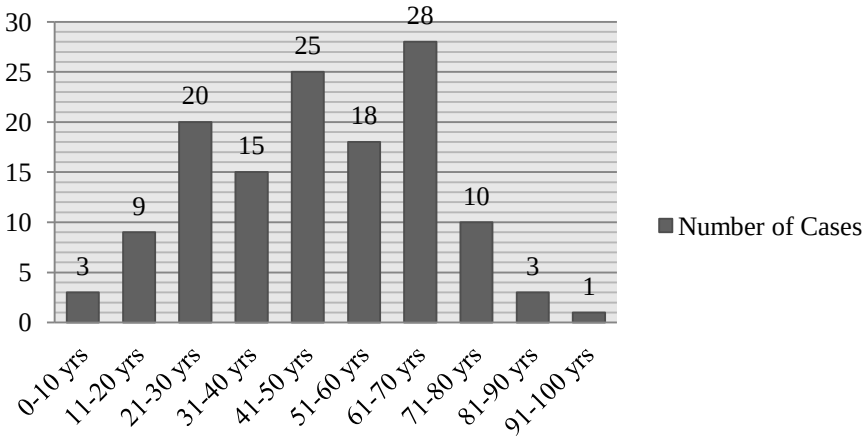

Figure 1: Age wise distribution of candiduria cases

Table 4: Antifungal susceptibility profile of the isolates

Species	AFST	AmphotericiB	Itraconazole	Ketoconazole	Fluconazole	Voriconazole
***C. albicans*(25)**	*S*	23	17	11	10	19
	SDD	2	3	3	3	1
	R	0	5	11	12	5
***C. tropicalis*(90)**	*S*	80	36	33	65	68
	SDD	10	44	25	8	8
	R	0	20	32	17	14
***C. glabrata* (2)**	*S*	0	0	0	1	2
	SDD	2	0	0	0	0
	R	0	2	2	1	0
***C. kefyr* (10)**	*S*	10	3	6	3	8
	SDD	0	5	1	2	0
	R	0	2	3	5	2
***C. krusei* (5)**	*S*	3	2	2	2	5
	SDD	2	1	1	0	0
	R	0	2	2	3	0

AFST- antifungal susceptibility test, S- sensitive, SDD- sensitivity dose dependent, R- resistant

IV. DISCUSSION

Nosocomial candidial UTI is fast gaining an important place in tertiary care hospitals. The significance of the presence of yeasts in urine of patients is not clearly understood [13]. A common clinical problem is deciding whether candiduria represents urinary tract infections or merely bladder colonization or contamination. Distinguishing contamination from true infection is not easy, despite the existence of reliable diagnostic criteria for significant candiduria. However, candiduria is sometimes a marker of disseminated candidiasis [10]. In the present study *C. tropicalis* 90/132(68.2%) was the most common candida isolated (Table 1). Studies suggest most frequent yeasts isolated from urine cultures as *C. albicans* followed by *C. glabrata* and *C. tropicalis* [11]. It is important to know the exact candida species before initiating antifungal treatment as few non albicans candida are inherently resistant to fluconazole [14]. In our study bladder catheterisation and antibiotic therapy have emerged as the commonest risk factors accounting for 48.9% of all the risk factors analysed. Urinary catheter serve as a portal of entry and most catheters become colonized if left for longer duration. Antibiotics increase the risk of colonization of candida species by suppression of endogenous flora and risk of candiduria increases with prolonged antibiotic use [15]. The susceptibility of yeasts to antifungal agents cannot always be predicted and therefore testing individual yeast pathogens against the appropriate antifungal agents is often necessary. Antifungal susceptibility testing *in vitro* ensures that the drug that will be chosen will be active against the infecting organism and therefore provide beneficial therapeutic effect to the patient under treatment. Antifungal susceptibility testing also aids in drug development studies and as a means of tracking the development of antifungal resistance in epidemiologic studies [16].

V. CONCLUSION

Based on the present study it is emphasised that there is the need of considering candiduria as an emerging and important entity in today's scenario. The presence of candiduria represents therapeutic challenge for physician and should be verified by the second clean catch urine culture. Since our study indicates the upcoming resistance of candida species to the antifungal agents in use, hence it is of utmost importance not only to identify candida up to species level but also to conduct its antifungal profile.

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