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REVALENCE AND ANTIFUNGAL SUSCEPTIBILITY PATTERNS OF YEAST ISOLATES IN A TERTIARY CARE CENTRE, SOUTH KERALA

Microbiology

Dr.jampala Srinivas* Associate Professor, Department Of Microbiology Heritage Institute Of Medical Sciences (hims) Gt Road Bypass, Varanasi Up----- 221311. *Corresponding Author

Miss Jean Infection Control Programmer Amrita Institute Of Medical Sciences (aims) Cochin, Kerala

ABSTRACT

Background: During recent years, fungal infections mainly yeast infections have raised exponentially leading to morbidity and mortality. Though Candida albicans was the predominant species, we are now encountering non- albicans Candida species (NAC) which are more pathogenic and highly antifungal resistant.

Aim: To study the prevalence and antifungal susceptibility patterns of yeast isolates in a tertiary care centre, south Kerala.

Methods: We retrospectively analyzed one and half year data obtained from different patients admitted to different departments.The clinical samples of patients were processed in Department of Microbiology for isolation and identification of fungi by using standard protocols over a period of one and half year data. The demographic data and risk factors for yeasts were evaluated.

Results: Out off 249 non-repeated yeast species, 90.76% were identified as Candida species and 9.23% (n=23) as non-Candida yeast species. C.albicans was the common isolate. We found a shift to Non albicans Candida (NAC). The clinical significance is emergence of NAC species with more pathogenecity and high level anti-fungal resistance.

Discussion: Our study reported 90.76% of Candida isolates and 9.2% of other yeast species.

Though C.albicans is the most common yeast, NAC group is slowly emerging as a virulent pathogen with multi- drug resistance.

Conclusion: Knowledge of epidemiology and anti-fungal pattern enables the clinicians to start the appropriate therapy and thereby decrease the morbidity and mortality.

KEYWORDS

Candida albicans, yeast, NAC, risk factors

INTRODUCTION

Yeasts are widely distributed in the environment and also form the part of the normal uently cause disease in man are the yeasts. The source of the yeast infection can be either endogenous or exogenous.1 The incidence of fungal infections has been on a rise in the last three decades with significant changes in their epidemiology. This is related to increasing size of immunocompromised immunosuppressive therapy, widespread use of antimicrobials and underlying diseases like AIDS, cancer. 2

Continuing increase in yeast infections is seen both in the community and nosocomial setting. The major hospital fungal pathogens consist of yeasts like Candida, Trichosporon spp etc. Candida species are the major fungal agents accounting for average mortality rate of 30%. 3-5 Infections caused by such fungi cause high morbidity and mortality in spite of using modern antifungal agents.6 Early initiation of appropriate antifungal therapy and improvement of immune function are the key factors for favorable outcome of fungal infections.

Hence knowledge of local epidemiology of yeast infections and their drug resistance patterns helps in devising appropriate management protocols which helps in effective control of fungal infections. With this background, we carried out one and a half year retrospective study to evaluate the incidence of yeast infections and their antifungal susceptibility pattern at a tertiary care hospital in South Kerala.

2.MATERIALS AND METHODS

2.1 Study design:

This is a retrospective analysis of one and half year data from January 2009-June 2010 about the yeast isolates at the Microbiology laboratory of Amrita Institute of Medical Sciences (AIMS), Kochi. The data was collected from the Laboratory Information System and case files. Institutional ethical clearance was obtained.

2.2. Samples

The data included yeast isolates from various clinical specimens submitted to the microbiology laboratory as part of routine lab diagnosis. Retrospectively relevant clinical information was collected and was added to the data bank.

For each episode, the following data was recorded; age, sex, in or out patient status, yeast identification, collection date and time and specimen from which yeast was isolated.

2.3 Microbiological Lab Diagnosis

Clinical specimens were collected from the patient depending upon the site of involvement under aseptic precautions and were analyzed by direct microscopy and culture as per standard laboratory procedures.7 Direct microscopic examination by potassium hydroxide (KOH [10% - 40%]) wet mount was done to observe budding yeast cells, hyphae and pseudohyphae. Smears for Gram staining were prepared to search for gram positive budding yeast cells. Indian ink preparation was done for csf samples when an encapsulated yeast was suspected.

Preliminary identification of the yeasts involved Gram staining, Indian ink staining and wet film microscopy. Samples were considered to be infected when gram stained smear shows more than five leukocytes per oil immersion field and more than five yeast cells with pseudohyphae. But in case of CSF, identification of any yeast cell plus five or more leukocytes was regarded as an infection.8

All the samples were cultured onto modified Sabouraud dextrose agar (SDA, Himedia Ltd, India) supplemented with antibacterial antibiotics (Chloramphenicol, gentamicin and/or tetracycline) and incubated at 250C & 370C. The seeded plates were examined for growth daily and considered to be negative when growth was not seen after 4 weeks of incubation. Preliminary identification was made by color and typical morphology of the colonies which were usually apparent within 24-48 hrs of incubation. The microscopy of such colonies showed hyphae, pseudohyphae and individual blastoconidia. The plates were sealed and stored at - 40C for further identification. The stored isolates were subsequently subcultured onto SDA to get pure growth and were identified to the species level by mini API ID 32 C test kit (bioMerieux, France). The tests were performed according to the manufacturer's instructions. Identification of these isolates was further confirmed by germ tube test and by microscopic examination of yeast morphology on cornmeal agar ("Dalmau Plate Culture" method).

Susceptibility of yeast species to antifungal drugs was determined using ATB FUNGUS 3 strip (bioMerieux, Marcy-l'Etoile, France) against flucytosine (5-FC), amphotericin B (AMB), fluconazole (FCA), itraconazole (ITR) and voriconazole (VRC) in a semisolid medium under conditions similar to the reference method for broth microdilution as described in the CLSI document M27-A3 (CLSI, 2008a).9

During the study period, a total of 249 non-repeated yeast species were isolated and analysed from various clinical specimens. Out of 249 isolates, 90.76% were identified as Candida species and 9.23% (n=23) as non-Candida yeast species (Table 1). Out of 226 Candida species, 73 (32.3%) were C.albicans and 153 (67.69%) were non-albicans Candida species (NAC spp.). Among 153 NAC spp., C.parapsilosis and C.tropicalis (n=57; 37.25% each) were the major isolates. T.asahii (n=8, 34.78%) other yeast species (n=23). followed by K.ohmeri (n=4, 17.39%) were found to be predominant isolates among other yeast species.

Higher rate of yeast infections were found more in men with male to female ratio 1.65. The median age of patients was 56.2 years (range = 4 months–88 years). Rate of yeast isolates was highest (n=109, 43.78%) in those aged 60 and above and lowest (n=12, 4.81) between the age group 11-20. Only 1.6% (n=4) of the samples were obtained from the age group below 1 year old (Table 2).

T.asahii and K.ohmeri were found to be the dominating yeast species in most of the age groups.

Table 1: showing distribution of Yeast species (n=249)

YEAST SPECIES	NUMBER (n)	PERCENTAGE (%)
CANDIDA SPECIES		
Non-albicans candida spp.	153	61.44
C.parapsilosis	57	22.9/ 37.25/25.22
C.tropicalis	57	22.9/ 37.25/25.22
C.krusei	10	4.01
C.sake	9	3.61
C.dubliniensis	7	2.81
C.glabrata	5	2.01
C.guilliermondii	4	1.6
C.famata	2	0.8
C.intermedia	2	0.8
C.albicans	73	29.32 / 32.3%
Total	226	90.76
OTHER YEAST SPECIES		
T.asahii	8	3.2 / 34.78
K.ohmeri	4	1.6 /17.39
Cr.neoformans	3	1.2
T.inkin	3	1.2
S.kluyverii	2	0.8
Geotrichum spp.	2	0.4
S.cerevisiae	1	0.4
Total	23	9.23
TOTAL	249	100

Table 2: Age and Gender-Wise Distribution of Yeast Species (n=249)

	Candida species n (%)	Other yeast species n (%)	Total number of isolates n (%)
0-10	12 (5.31)	0 (0)	12 (4.81)
11-20	3 (1.33)	1 (4.35)	4 (1.60)
21-30	10 (4.42)	3 (13.04)	13 (5.22)
31-40	15 (6.64)	0 (0)	15 (6.02)
41-50	28 (12.38)	2 (8.70)	30 (12.05)
51-60	64 (28.32)	2 (8.70)	66 (26.51)
>60	94 (41.60)	15 (65.21)	109 (43.78)
Total	226 (100)	23 (100)	249 (100)
GENDER			

	Number of isolates	Percentage (%)
Males	155	62
Females	94	38
Total	249	100

Yeasts were isolated mainly from tissue (n=107, 43%), the respiratory tract (n=87, 35%) and nail (n=34, 13.65%) and from the remaining five specimens (2.8%) which include bone and stool in 0.8% each and ear swab, pus and high vaginal swab in 0.4% each. The most predominant species in the tissue samples were C.parapsilosis (34, 31.8%), C.tropicalis (31, 29%) and C. albicans (17, 15.9%). The most prevalent species isolated from respiratory samples were C. albicans (50, 57.5%) followed by C.tropicalis (16, 18.4%) were C. parapsilosis (13, 38.23%) was the most common species isolated from nail. C. tropicalis was the most frequent species isolated from the urine (3, 50%) followed by C. albicans, C. parapsilosis and C. glabrata with isolation rate of 16.66% each. C.neoformans (3, 60%) and C. parapsilosis (2, 40%) were most common yeast isolates from CSF and that from blood were C. parapsilosis (2, 66.66%) and C.tropicalis (1, 33.33%). T.asahii, K.ohmeri, Cr.neoformans, T.inkin / S.kluyverii, Geotrichum spp. and S.cerevisiae were the common non-Candida yeast isolates.

Table 3: Distribution of yeast species according to various clinical specimens

Yeasts isolated	Clinical specimens (N (%)							
	Tissue	RS*	Nail	Urine	CSF	Blood	Others	Total
C. albicans	17 (15.9%)	50 (57.5%)	3 (8.82%)	1 (16.7)	0	0	2(28.6%)	73(29.32%)
C. parapsilosis	34 (31.8%)	2(2.3%)	13(38.23%)	1(16.66%)	2(40%)	1(33.33%)	4(57.1%)	57(22.9%)
C.tropicalis	31(29%)	16(18.4%)	5(14.7%)	3(50%)	0	2(66.66%)		57(22.9%)
C. krusei	2(1.9%)	6(6.9%)	2(5.9%)	0	0	0		10(4.01%)
C. sake	6(5.6%)	2(2.3%)	1(2.94%)	0	0	0		9(3.61%)
C.dubliniensis	0	6(6.9%)	0	0	0	0	1(14.3%)	7(2.81%)
C. glabrata	2(1.9%)	2(2.3%)	0	1(16.66%)	0	0		5(2.01%)
C.guillermondii	0	2(2.3%)	2(5.9%)	0	0	0		4(1.61%)
C. famata	1(0.93%)	0	1(2.94%)	0	0	0		2(0.8%)
C.intermedia	1(0.93%)	0	1(2.94%)	0	0	0		2(0.8%)
T.asahii	5(4.67%)	0	3(8.82%)	0	0	0		8(3.21%)
K.ohmeri	4(3.73%)	0	0	0	0	0		4(1.61%)
T.inkin	1(0.93%)	0	2(5.9%)	0	0	0		3(1.20%)
C.neoformans	0	0	0	0	3(60%)	0		3(1.20%)
S.kluyverii	2(1.9%)	0	0	0	0	0		2(0.8%)
S.cerevisiae	0	0	1(2.94%)	0	0	0		1(0.4%)
Geotrichum spp	1(0.93%)	1(1.15%)	0	0	0	0		2(0.8%)
Total	107 (43%)	87 (35%)	34 (13.6%)	6 (2.4%)	5 (2%)	3 (1.2%)	7 (2.8%)	249 (100%)

RS*= Respiratory specimens which include Bronchoalveolar lavage, Bronchial washing, Tracheal aspirate, expectorated sputum, Endotracheal Suction Tip. Others**= Bone, Stool, Ear swab, Pus, High vaginal swab. N = number of specimens.

Table 4: Distribution of yeast species according to various clinical departments

Clinical Departments (N (%))													
Yeasts Isolated	Endo-Crinology	Pulmo-Nology	Derma-Tology	General Medicine	Paedia-Trics	General surgery	Onco-logy	Cardio-logy	ENT*	O.B.G**	Neuro-logy	Uro-Logy	Total
C. albicans	14(5.6)	41(16.5)	2 (0.8)	5(2)	4(1.6)	2(0.8)	2(0.8)	1(0.4)	1(0.4)	1(0.4)			73(29.3)
C. parapsilosis	32(13)	1(0.4)	13(5.2)	3(1.2)	1(0.4)	1(0.4)	2(0.8)	2(0.8)	2(0.8)				57(22.9)
C.tropicalis	23(9.2)	7(2.8)	5(2)	2(0.8)	2(0.8)	4(1.6)	2(0.8)	2(0.8)	2(0.8)	3(1.2)	1(0.4)	4(1.6)	57(22.9)
C. krusei	2(0.8)	6(2.4)	2(0.8)										10(4)
C. sake	6((2.4)	1(0.4)	1(0.4)		1(0.4)								9(3.6)

C. dublinensis		4(1.6)		1(0.4)	1(0.4)					1(0.4)			7(2.8)
C. glabrata	2(0.8)	2(0.8)		1(0.4)									5(2)
C.guillermondii		1(0.4)	2(0.8)			1(0.4)							4(1.6)
C. famata	1(0.4)		1(0.4)										2(0.8)
C. intermedia	1(0.4)		1(0.4)										2(0.8)
T.asahii	5(2)		3(1.2)										8(3.2)
K.ohmeri	4(1.6)												4(1.6)
T.inkin	1(0.4)		2(0.8)										3(1.2)
C.neoformans											3(1.2)		3(1.2)
S.kluyverii	2(0.8)												2(0.8)
S.cerevisiae		1(0.4)											1(0.4)
Geotrichum spp	2(0.8)												2(0.8)
Total	95 (38.2)	64(25.7)	32(13)	12(4.8)	9 (3.6)	8(3.2)	6(2.4)	5(2%)	5(2)	5(2%)	4(1.6)	4(1.6)	249

#Data are presented as No. (%). *Ear Nose and Throat. **Obstetrics and Gynaecology

Almost all the species of Candida showed 100% sensitivity to flucytosine except C.tropicalis (93%). The Candida isolates like C.albicans, C.parapsilosis, C.tropicalis and C.krusei showed below 70% sensitivity to Fluconazole while other Candida species were 100 percent sensitive. Other yeast species showed similar pattern.

DISCUSSION

Species differentiation of yeasts facilitates the understanding of their epidemiology particularly regarding the reservoir and mode of transmission. This helps in devising effective measures to prevent and control transmission of resistant fungal pathogens. Infections due to yeast pathogens are associated with high mortality because of rising trend in antifungal resistance.

A total of 249 non-repeated yeast species were isolated during the study period. Of that 90.8% were identified as Candida species and 9.2% as other yeast species. Among the Candida species, C.albicans was found to be predominant isolate followed by C.parapsilosis and C.tropicalis. While T.asahii (3.2%) and K.ohmeri (1.6%) represent major isolates among non-candida yeast infections.

Kucukates et al. 10 and Zer et al.11 reported that the major isolate was C.albicans followed by C.parapsilosis and C.tropicalis. Retrospective analysis of yeast isolates by Hamid et al 12 showed C.albicans (28.6%), as major isolate. In all the above studies, the species of higher isolation rate was found to be C.albicans which holds true in our study also. However isolation rate of C.albicans (29.3%) in present study matches closely with that of C.albicans (28.6%) in a study by Hamid et al. 12

Though the reports in Indian literature 13, 14 showed C.albicans as a major clinical isolate, recent studies 15,16,17 reported an increase in the prevalence of non-albicans Candida (NAC) species. The present study reported C.parapsilosis and C.tropicalis as predominant NAC spp.

Thus there is a progressive shift from a predominance of C.albicans to NAC species mainly C. tropicalis, C. parapsilosis, C.krusei and C.glabrata.

NAC species also demonstrated the production of virulence factors once attributed to C.albicans. Non-albicans Candida demonstrated high resistance to azole group of antifungal agents. Therefore, it can be concluded that non-albicans Candida species have emerged as an important cause of infections. Their isolation from clinical specimen can no longer be ignored as a contaminant or commensal.

We noticed a significant relationship between incidence of yeast infections and age in this study. The majority of the patients were in old people and this might be related to aging, age-associated physiological changes and comorbidities.In present study we found that the age of the study population ranged from 4 months to 88 years with the mean age of 56.2 years similar to previous reports.

Maximum incidence of yeast infections is seen in patients aged over 60. We found similar results in our study showing a high rate of yeast infections in patients of similar age group.

The high incidence of yeast infections in older age group might be related to aging, age-associated physiological changes like immunosenescence, multiple drug use and comorbidities.

Polypharmacy represents a major problem for older people as aging leads to different disease states and so requires multiple medications. Polypharmacy is associated with drug-interactions, medication non-adherence and drug-induced liver injury. Sex distribution in present study showed that males are more commonly affected.

The varied distribution of yeast infections in relation to age, gender and risk factors is attributed to socio-economic and geo-epidemiological differences, comorbidities and threat of emerging antifungal-resistant strains of yeast species.

Knowledge of risk factors for yeast infections may help to identify those patients who could benefit from early antifungal therapy

The most common risk factors associated with yeast infections in our study were broad spectrum antibiotic therapy, followed by catheterization and diabetes mellitus. Highest number of isolates was obtained from Endocrinology department followed by Pulmonology and Dermatology. All patients of Endocrinology were diagnosed to have Type 2 Diabetes Mellitus. In case of diabetic patients non-healing ulcers, cellulites and gangrene contributed to be the major risk factors. The present study showed a higher rate of recovery from tissue followed by respiratory tract specimens and nail. The predominant yeast species isolated from tissue were C.parapsilosis and C.tropicalis. Identification of yeasts to the species level is important information for the physician, in part because of the changing susceptibility patterns that are now seen.

Candida krusei is intrinsically resistant to fluconazole. Variable susceptibility with fluconazole is noted for C. glabrata, C. parapsilosis, C.rugosa, C. tropicalis, Saccharomyces cerevisiae, and Trichosporon cutaneum.23, 24 One study revealed decreased susceptibility to fluconazole, itraconazole and Amphotericin B in C. glabrata and C. krusei isolates.25

Amphotericin B along with flucytosine showed excellent antifungal activity in case of yeasts other than candida species. .

Except for some yeast isolates, our study showed 100% susceptibility to *fluconazole.* However our study exhibits *fluconazole* resistance in some isolates of *C.tropicalis, C.albicans, C.parapsilosis and mainly C.krusei* despite of in- vitro susceptibility, *C.krusei* is always reported to be resistant to *fluconazole* as the species is inherently resistant to it. Prolonged use of *fluconazole* like long term prophylaxis accounted for its intrinsic resistance in *C.krusei.*

The cause of *fluconazole* resistance in *C.krusei is* by inhibiting *cytochrome* P450 dependent conversion of *lanosterol* to ergosterol. Ergosterol is the main sterol in the cell membrane of fungi. This leads to accumulation of 14methyl *sterols* and depletion of membrane associated ergosterol, altering cell membrane properties and function, and resulting in inhibition of cell growth and replication. 26 Due to relative resistance to many anti-fungal agents and capability of nosocomial transmission makes *C. krusei* a major nosocomial pathogen in hospitals.27, 28

The results of our study were in accordance with the 8.5-year global

surveillance of susceptibilities of Candida and non-Candidal yeasts which demonstrated that *fluconazole* was very active against Candida species including *C.albicans, C.parapsilosis, C.tropicalis, C.lusitaniae* and less active against other Candida spp. 29

Among the candida isolates, *itraconazole* was more active against *C.parapsilosis* (93% S) and among non-candidal yeast isolates, the drug showed 100% susceptibility against *Cr.neoformans* amd *Geotrichum* spp

Pfaller MA et al. (2007) 29 reported that with the exception of *C.glabrata, itraconazole* was moderately active against most medically important *fluconazole-susceptible* and resistant Candida species and the very same was also seen in our study.

These results are also similar to the results obtained from the study carried out by *Groll* et al. in which itraconazole exerted fungicidal activity against some strains of *Cr.neoformans* and is generally *fungistatic* against many types of yeast.

Among the candida isolates, *itraconazole* was more active against C.parapsilosis (93% S) and among non-candidal yeast isolates, the drug showed 100% susceptibility against *Cr.neoformans* amd *Geotrichum* spp

Pfaller MA et al. 25 reported that with the exception of *C.glabrata, itraconazole* was moderately active against most of the medically important yeasts. *C. glabrata* may be dose-dependent susceptible, up to 15% may exhibit true resistance.30

Groll AH et al. reported that *voriconazole* exerted fungicidal (2007) activity against most yeast like non-albicans Candida spp. and *Cr.neoformans. Pfaller* et al. 29 observed that *voriconazole* was active against all Candida spp., including fluconazole-resistant *C.albicans, C.glabrata,* and *C.krusei, Cr.neoformans* and most *Trichosporon* spp., including *T.asahii.*

Both the isolates of *S.kluyverii* were resistant to amphotericin B, *fluconazole, itraconazole* and *voriconazole* and were susceptible only to flucytosine. Being a retrospective study the clinical significance of *S.kluyverii,* a plant pathogen, could not be determined.

CONCLUSION

To conclude species level identification of yeast isolates and their sensitivity profile and knowledge
of emerging yeast isolates will enable clinicians to choose appropriate antifungal agents, thus decreasing patient's morbidity and mortality.

REFERENCES

1. Vaudry WL, Tierney AJ, Wenman WM. Investigation of a cluster of Candida albicans in a neonatal intensive care unit. J Infect Dis 1988; 158: 1376-1379.
2. Walsh TJ, Groll A, Hiemenz J, Fleming R, Roilides E, Anaissie E. Infections due to emerging and uncommon medically important fungal pathogens. Clin Microbiol Infect. 2004 Mar;10 Suppl 1:48–66.
3. Pfaller MA, Diekema DJ. Epidemiology of invasive candidiasis: a persistent public health problem. Clin Microbiol Rev 2007; 20:133–163.
4. Costa-de-Oliveira S, Pina-Vaz C, Mendonça D, Gonçalves Rodrigues A. A first Portuguese epidemiological survey of fungaemia in a university hospital. Eur J Clin Microbiol Infect Dis. 2008 May;27(5):365–74.
5. Pappas PG, Rex JH, Lee J, et al. Prospective observational study of candidemia: epidemiology, therapy, and influences on mortality in hospitalized adult and paediatric patients. Clin Infect Dis 2003; 37:634–643.
6. Perlroth J, Choi B, Spellberg B. Nosocomial fungal infections: epidemiology, diagnosis, and treatment. Med Mycol. 2007 Jun;45(4):321–46.
7. Jagadish Chander, Medical Mycology, 2nd edition, New Delhi, Mehta Publishers, 2002; 7.
8. *Feglo P. Prevalence and Antifungal Susceptibility Patterns of Yeast Isolates at the Komfo Anokye Teaching Hospital (KATH), Kumasi, Ghana. British Microbiology Research Journal. 2012 Jan 10;2(1):10–22.*
9. Clinical and Laboratory Standards Institute. *Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts: Approved Standard. 3rd edn.* Clinical and Laboratory Standards Institute; Wayne, PA: 2008. Document M27-A3
10. *Kucukates E, Erturan Z, Susever S, Yegenoglu Y. In vitro susceptibility of yeasts isolated from patients in intensive care units to fluconazole and amphotericin B during a 3-year period. APMIS. 2005 Apr;113(4):278–83.*
11. *Zer Y, Balci I, Meriç G. Identification and antifungal susceptibility of Candida isolated from intensive care unit patients. New Microbiol. 2002 Oct;25(4):489–94.*
12. *Hamid ME, Assiry MM, Joseph MR, Haimour WO, Abdelrahim IM, Al-Abed F, et al. Candida and other yeasts of clinical importance in Aseer region, southern Saudi Arabia. Presentation of isolates from the routine laboratory setting. Saudi Med J. 2014 Oct;35(10):1210–4.*
13. Pahwa N, Kumar R, Nirkhiwale S, Bandi A. Species distribution and drug susceptibility of candida in clinical isolates from a tertiary care centre at Indore. Indian J Med Microbiol. 2014 Mar;32(1):44–8.
14. Sundaram J, Sivan R, Sukumaran J. Changing trend in the clinical distribution of Candida species in a tertiary care hospital. Journal of Dr NTR University of Health Sciences. 2012;1(4):222.
15. Mohandas V, Ballal M. Distribution of Candida species in different clinical samples and their virulence: biofilm formation, proteinase and phospholipase production: a study on hospitalized patients in southern India. J Glob Infect Dis. 2011 Jan;3(1):4–8.
16. Deorukhkar SC, Saini S, Mathew S. Non- albicans Candida Infection: An Emerging Threat. Interdisciplinary Perspectives on Infectious Diseases. 2014;2014:1–7.
17. Oberoi JK, Wattal C, Goel N , Raveendran R, Datta S, Prasad K. Non- albicans Candida species in blood stream infections in a te r tiary care hospital at New Delhi, India.Indian J Med Res. 2012 Dec;136 (6) : 997–1003.
18. 1,3,4
19. Mokaddas EM, Al-Sweih NA, Khan ZU. The species distribution and the antifungal susceptibility of Candida bloodstream isolates in Kuwait: A 10 year study. J Med Microbiol 2007; 56: 255-9.
20. Chakraborti A, Ghosh A, Batra R, Kaushal A, Roy P, Singh H. Antifungal susceptibility patterns of the non-albicans Candida species and the distribution of the species which were isolated from candidaemia cases over a 5 year period. Indian J Med Res 1996; 104: 171-6.
21. Dr.Parimal, H.Patel, Dr.Jayshree, Dr.P.D. Shah, Dr.Sanjay Rathod, Dr.Lata R. Patel, et al. Prevalence and Antifungal Susceptibility Profiles of Candida tropicalis in a Tertiary Care Hospital Ahmedabad, Gujarat, India International Journal of Scientific Research, Vol.II, Issue.III March 2013.
22. Pahwa N, Kumar R, Nirkhiwale S, Bandi A. Species distribution and drug susceptibility of candida in clinical isolates from a tertiary care centre at Indore. Indian J Med Microbiol. 2014 Mar;32(1):44–8.
23. Hazen KC. New and emerging yeast pathogens. Clin Microbiol Rev. JAMA. 1995;8:462–478.
24. Hazen KC, Howell, SA. Candida, Cryptococcus and other yeasts of medical importance. Manual of Clinical Microbiology, 8th Ed. Location: ASM Press; 2003:1693–1711.
25. Pfaller MA, Diekema DJ, Jones RN, et al. Trends in antifungal susceptibility of Candida spp. isolated from pediatric and adult patients with blood stream infections. SENTRY Antimicrobiol Surveillance Program 1997 to 2000. J Clin Microbiol. 2002;40:852–856.
26. Groll AH, Piscitelli SC, Walsh TJ. Antifungal Pharmacodynamics: Concentration-Effect Relationships in Vitro and in Vivo. Pharmacotherapy. 2001 Aug;21(8 Part 2):133S – 148S
27. Gill K, Kumar S, Xess I, Dey S. Novel synthetic anti-fungal tripeptide effective against Candida krusei. Indian J Med Microbiol. 2015 Mar;33(1):110–6
28. Brillowska-Dabrowsha A, Siniecka A. Molecular detection of Candida krusei. Int Res J Microbiol 2012;3:275-7.
29. *Pfaller MA, Diekema DJ, Gibbs DL, Newell VA, Meis JF, Gould IM, et al. Results from the ARTEMIS DISK Global Antifungal Surveillance study, 1997 to 2005: an 8.5-year analysis of susceptibilities of Candida species and other yeast species to fluconazole and voriconazole determined by CLSI standardized disk diffusion testing. J Clin Microbiol. 2007 Jun;45(6):1735–45.*