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Epidemiology of Candida Infections among High Risk Neonates and Infants from a Tertiary Care Setting of North India

Sarver Jahan[1]*, Abida Malik[1], Nazish Fatima[1], S Manazir Ali[2] and Mohd Waseeque Khan[3]

[1]Department of Microbiology, JNMC, AMU, Aligarh, India
[2]Paediatrics, JNMC, AMU, Aligarh, India
[3]Paediatric, ELMCH, Lucknow, India

***Corresponding Author**: Sarver Jahan, Department of Microbiology, JNMC, AMU, Aligarh, India.*

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Abstract:

Introduction: In recent years, fungal infections have risen exponentially and are a cause of significant morbidity and mortality especially in high risk babies. Although *Candida albicans* remains the most common fungal isolate from neonatal candidemia, longitudinal studies have detected a shift towards non-albicans Candida (NAC) species.

Objective: To study the risk factors, prevalence, virulence determinants and antifungal susceptibility pattern of candidiasis among high risk neonates and infants.

Materials and Methods: Samples were collected aseptically from 128 high risk neonates and infants admitted in the NICU and HDU at JNMCH, Aligarh from February 2013 to October 2014. They were cultured and identified by standard microbiological techniques. Virulence factors were tested as mentioned. Antifungal susceptibility testing was performed according to CLSI guidelines.

Results: Of the 128 neonates and infants studied 89 (69.5 %) had septicaemia, 14(10.9 %) had oral thrush and 12 (9.4 %) had urinary tract infections. In our study, we found 39 cases from which 49 isolates of *Candida* were taken from different specimen. Of the 39 candidiasis cases *Candida albicans* (59.2%) was the most common species isolated while non albicans Candida (NAC) were 40.8% (*C. tropicalis* 14.3%, *C. parapsilosis* 12.2%, *C. guilliermondii* 6.2%, *C. glabrata* 4%, *C. krusei* 2% and *C. dubliniensis* 2%). The significant associated risk factors in these infections were broad spectrum antibiotic therapy (100%), presence of peripheral catheter (100%), low birth weight (76.9%) and hospital stay of more than 7 days (76.9%). All the virulence markers were significantly present in the Candida isolates among neonates and infants. Resistance to fluconazole, ketoconazole, clotrimazole was observed in 10.3%, 10.3%, 6.8% isolates of C. albicans respectively. Resistance to fluconazole, clotrimazole and amphotericin B was observed in 15%, 20%, 16.7% isolates of NAC respectively. No resistance was observed against itraconazole and nystatin. The maximum mortality was found in patients with NAC infections (52.9%) in comparison to C. albicans infection (31.8%).

Conclusion: There is a considerable increase in Candida infections especially with NAC in neonates and infants with more resistance towards antifungal drugs. Presence of broad spectrum antibiotic, peripheral venous catheter, low birth weight and prolonged hospital stay were found to be the significant risk factors.

Keywords: *Candida albicans; Non albicans Candida; High risk neonates; Infants*

Introduction

Candidiasis is the commonest fungal disease found in human affecting mucosa, skin, nails and internal organs. Candida species constitute the fourth most common pathogen isolated among nosocomial blood stream infections [1,2].

Candida affects a large population of neonates and infants especially high risk babies [3,4]. These babies regardless of birth weight, size or gestational age, have a greater than average chance of mortality or morbidity, especially up to one year of life. Premature infants

are a high risk group notably due to their undeveloped immune systems. Candida spp. may be acquired vertically from the mother, or horizontally in the neonatal intensive care unit [5]. Candida spp. are considered as opportunistic pathogens because they possess many virulence factors which contributes in the pathogenesis of Candida infections. The virulence of Candida spp. is attributed to certain factors like adherence, biofilm formation, and the production of tissue damaging extracellular hydrolytic enzymes [6,7]. Extracellular hydrolytic enzymes like phospholipase and proteinase are important for colonization and invasion of host tissue [8].

The increased isolation rates of non albicans Candida species and a gradual shift in the antifungal susceptibility profile have underlined the need to monitor laboratory data for possible emergence of resistance and to select most appropriate antifungal agent for therapy.

Taking into consideration the above mentioned facts, the present study was undertaken with the following aims and objectives.

- To isolate and characterize the Candida species from the infections of neonates and infants.
- To study the virulence determinants of Candida species.
- To study the antifungal susceptibility pattern of the isolates.
- To study the clinical presentations in relation to Candida spp.
- To determine the risk factors for candidiasis in the study group.

Materials and Methods

The present study was carried out in the Department of Microbiology J. N. Medical College, AMU, on 128 high risk neonates and infants admitted in the NICU and in the HDU of Department of Paediatrics, during the period of one and half years from 2013 to 2014. Various clinical specimens including blood, tracheobronchial aspirate, oral swab, ear swab, CSF and urine were collected. Demographic and clinical data such as age, sex, birth weight, antibiotic prophylaxis, presence of CVC, and clinical outcome of the neonates were noted.

Specimens like endotracheal aspirate, urine, oral swab etc., were subjected to direct microscopy by making a lactophenol cotton blue (LCB) mount and /or a Gram stained smear. The samples were inoculated on to Sabouraud's dextrose agar as the main isolation medium. For blood samples, approximately 1 to 2 ml of blood was collected under aseptic precautions and inoculated in biphasic brain heart infusion medium. The culture medium was incubated at 37°C for a week or longer if required. Subculture was done on third, fifth, and seventh day. All the Candida isolates were subjected to germ tube test using normal human serum. Colonies were identified up to the species level on the basis of colony characteristics, morphology on Corn meal agar, growth on Hi- CHROME Candida agar, carbohydrate fermentation, and assimilation patterns [9,10]. The procedure followed was in accordance with the ethical standards of the responsible committee and informed written consent was taken prior to every procedure.

Detection of various virulence factors:

Biofilm production:

Biofilm production of isolates was demonstrated with a slight modification of the method, as described by Hassan *et al*., [11].

Proteinase activity:

To determine proteinase activity, bovine-serum albumin agar defined by Staib [12] was employed.

Phospholipase activity:

For phospholipase, the egg yolk agar method of Price., *et al*. [13] which was modified by Samaranayake., *et al.* [14], was employed.

Phospholipase activity (Pz) and proteinase activity were calculated by dividing the diameter of the colony by the diameter of the colony plus precipitation zone.

Haemolysin activity:

Haemolysin activity of Candida spp. was detected by blood agar plate assay as described by Manns., *et al*. [15] a transparent/ semi-transparent zone around the inoculation site was considered as positive hemolytic activity.

Pseudohyphae formation:

Pseudohyphae formation against blastospores, was determined by microscopy counting in a liquid medium containing RPMI 1640 (Sigma) and fetal bovine serum [16].

All the isolates were screened for antifungal susceptibility testing by the Disk Diffusion method modified by Chakrabarti., *et al*. [17] using yeast nitrogen base-glucose (YNBG) agar. The antifungal agents tested were Amphotericin B, Nystatin, Ketoconazole, Clotrimazole, Fluconazole and Itraconazole (HiMedia Laboratories, Mumbai, India). The broth micro dilution-minimum inhibitory concentration (BMD-MIC) of the isolates was performed for the fluconazole, ketoconazole and amphotericin B using RPMI medium and MOPS buffer. MIC results were interpreted as per NCCLS (M27-A2) [18] guidelines. Isolates showing fluconazole MIC ≤ 8 µg/ml were regarded as susceptible, 16 - 32 µg/ ml as dose-dependent susceptible and ≥ 64 µg/ml as resistant. The quality control test was performed by using the strains of *Candida parapsilosis* (ATCC 22019), *Candida krusei* (ATCC 6258) and *Candida albicans* (ATCC 90028).

Statistical Methods

The 'chi-square' test and the Student's 't' test were used to compare the data. A 'p' value of < 0.05 was taken as indicative of statistical significance, and a 'p' value of < 0.01 was considered highly significant.

Results

Of the 128 neonates and infants 89 (69.5 %) were septicaemia cases followed by oral thrush in 14 (10.9 %) cases and urinary tract infections in 12 (9.4 %) cases. Other presentation included in the study were chronic suppurative otitis media (CSOM) (3.9%), pneumonia (3.1%) and meningitis (3.1%) (Table 1).

Clinical diagnosis	No. of patients	%
Septicaemia	89	69.5
UTI	12	9.4
Oral thrush	14	10.9
Pneumonia	4	3.1
Meningitis	4	3.1
CSOM	5	3.9
Total	128	100

Table 1: *Distribution of neonates and infants according to clinical diagnosis (n=128).*

The most frequent risk factors in this study population included broad spectrum antibiotic therapy in 112 (87.5%) neonates and infants followed by presence of peripheral catheter in 95 (74.2%) neonates and infants. Other important risk factors found were vaginal delivery in 93 (72.7%), low birth weight in 82 (64%) and duration of hospital stay of more than 7 days in 79 (61.7%) cases. Additional risk factors among neonates included total parenteral nutrition, prematurity, presence of endotracheal tube, intake of steroid and ventilator support. Among candidiasis patients broad spectrum antibiotic therapy (100%), presence of peripheral catheter (100%), low birth weight (76.9%), hospital stay of more than 7 days (76.9%) and vaginal delivery (89.7%) were significantly associated risk factors (Table 2).

Risk factors	Neonates and infants with candidiasis (n=39)		Neonates and infants without candidiasis (n=89)		P value
	No.	%	No.	%	
Paediatrics factors					
Prematurity	18	46.1	42	47.1	NS
Low birth weight	30	76.9	52	58.4	0.0483(S)
Steroid intake	6	15.3	13	14.6	NS
Broad spectrum antibiotic	39	100	73	82	0.002(S)
Total Parenteral Nutrition	18	46.1	25	28	NS
Peripheral Catheter	39	100	56	63	0.0001(S)
Endotracheal tube	7	17.9	11	12.3	NS
Ventilator support	7	17.9	12	13.5	NS
Duration of hospital stay	30	76.9	49	55	0.029(S)
Maternal factors					
Vaginitis in third trimester	12	30.7	31	34.8	NS
Vaginal delivery	35	89.7	58	65.2	0.0046(S)
Antibiotic intake in 3rd trimester	8	20.5	28	31.4	NS

Table 2: *Risk factors for candidiasis among neonates and infants in the study group.*

Out of total 128 patients, Candida was isolated in 39 (30.5%) cases. From 39 cases 49 samples were collected from different sites. *Candida albicans* (59.2%) was the most common species isolated while non albicans Candida (NAC) were 40.8% (*C. tropicalis* 14.3%, *C. parapsilosis* 12.2%, *C. guilliermondii* 6.2%, *C. glabrata* 4%, *C. krusei* 2% and *C. dubliniensis* 2%) (Figure 1) (Table 3).

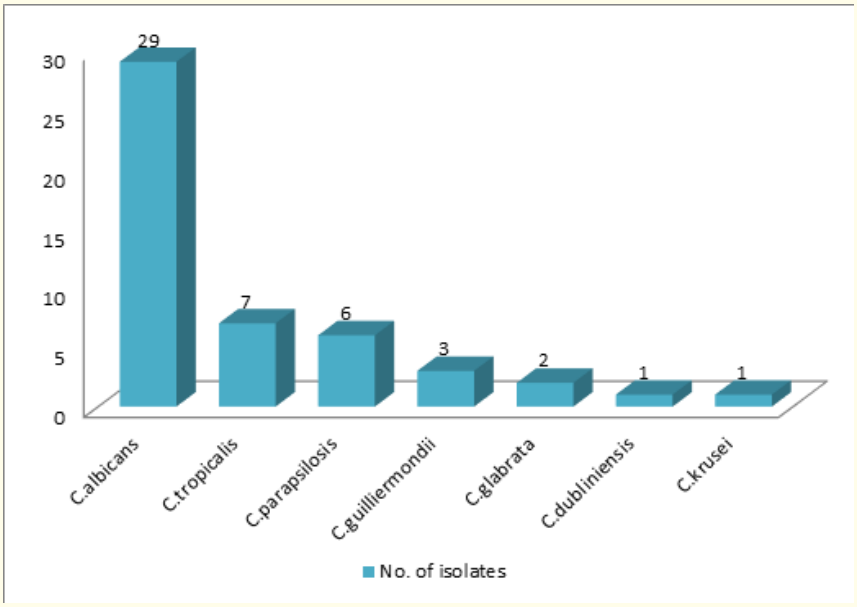

Figure 1: *Candida spp. isolated from patients in the study group.*

Clinical diagnosis	No. of. patients	Sample	No. of. isolates	%
Septicaemia	25	Blood (23)	29	59.2
		blood (3) +urine (3) *		
		blood (3) +oral swab (3) *		
Oral thrush	5	Oral swab	5+3*=8	16.3
UTI	4	Urine	4+3*=7	14.3
CSOM	2	Ear swab	2	4.1
Meningitis	2	CSF	2	4.1
Pneumonia	1	Endotracheal aspirate	1	2
Total	39		49	100

**3 urine and 3 oral swab Candida isolates were from septicaemia patients.*

Table 3: *Distribution of Candida isolates in relation to clinical diagnosis in neonates and infants with candidiasis.*

All the virulence markers were significantly present in the Candida isolates among neonates and infants. However, among all the factors, biofilm and hemolysin production were found to be highly significant ($p < 0.01$) (Table 4).

Virulence Factor	Positive	Negative	'P' value
Biofilm formation	43	6	0.0001(S)
Phospholipase production	17	32	0.004(S)
Proteinase production	19	30	0.042(S)
Hemolysin production	49	0	0.0001(S)
Pseudohyphae formation	10	39	0.0001(S)

Table 4: *Presence of various virulence markers among Candida isolates.*

Resistance to fluconazole, ketoconazole, clotrimazole was observed in 10.3%, 10.3%, 6.8% isolates of C. albicans respectively. Resistance to fluconazole, clotrimazole and amphotericin B was observed in 15%, 20%, 16.7% isolates of NAC respectively. No resistance was observed against itraconazole and nystatin (Table 5).

Candida spp.	No. of. isolates	Clotrimazole		Fluconazole		Ketoconazole		Amphotericin B		Itraconazole		Nystatin	
		S	R	S	R	S	R	S	R	S	R	S	R
C.albicans	29	27 (93.1)	2 (6.8)	26 (89.7)	3 (10.3)	26 (89.7)	3 (10.3)	29 (100)	0	29 (100)	0	29 (100)	0
C.tropicalis	7	5 (71.4)	2 (28.6)	6 (85.7)	1 (14.3)	7 (100)	0	7 (100)	0	7 (100)	0	7 (100)	0
C.parapsilosis	6	6 (100)	0	6 (100)	0	6 (100)	0	5 (83.3)	1 (16.7)	6 (100)	0	6 (100)	0

C.guilliermondii	3	2 (66.7)	1 (33.3)	3 (100)	0	3 (100)	0	3 (100)	0	3 (100)	0	3 (100)	0
C.glabrata	2	2 (100)	0	2 (100)	0	2 (100)	0	2 (100)	0	2 (100)	0	2 (100)	0
C.dubliniensis	1	1 (100)	0	0	1 (100)	1 (100)	0	1 (100)	0	1 (100)	0	1 (100)	0
C.krusei	1	0	1 (100)	0	1 (100)	1 (100)	0	1 (100)	0	1 (100)	0	1 (100)	0
Total	49	43 (87.8)	6 (12.2)	43 (47.8)	6 (12.2)	46 (93.9)	3 (8.1)	48 (98)	1 (2)	49 (100)	0	49 (100)	0

Figures in parenthesis indicate percentage

Table 5: *Antifungal susceptibility pattern of various Candida spp. by disc diffusion method.*

Overall, the incidence of mortality in patients with Candida infection was 41 %.

Mortality was associated with almost all the species of Candida, out of which infection with non albicans Candida showed higher mortality (52.9%) as compared to *C. albicans* (31.8%).

Individually among non albicans Candida infection higher mortality was seen by *C. tropicalis*, *C. guilliermondii* and *C. glabrata* (11.8% each) (Table 6).

Candida spp.		No. of cases		Mortality		%	
C. albicans		22		7		31.8	
C. parapsilosis	Non albicans Candida	5	17	1	9	5.9	52.9
C. tropicalis		5		2		11.8	
C. guilliermondii		3		2		11.8	
C. dubliniensis		1		1		5.9	
C. krusei		1		1		5.9	
C. glabrata		2		2		11.8	
Total		39		16		41	

Table 6: *Outcome of patients with candidiasis (n=39).*

Discussion

A total of 128 children suffering from various clinical diseases, categorized into different predefined high risk groups were included in the study to determine the profile of Candida infections with respect to the predominant species, pathogenic characteristics and antifungal susceptibility analysis of the isolates in high risk neonates and infants.

Among the patients in whom Candida was isolated, the most common group was neonates and infants with septicaemia (59.2%). The other major patients group with candidiasis included those with oral thrush (16.3%), UTI (14.3%), meningitis (4.1%), ear infection (4.1%), pneumonia (2%). This is in agreement with the findings of Altuncu E., *et al*. [19].

Overall the rate of Candida isolation from various specimens in our study group was 30.5%. *C.albicans* formed the largest group (59.2%) of Candida species isolated in this study. Jarvis [20] and Pfaller [21] had reported 50 to 70% Candida albicans isolation, Wingard

[22] 54% isolation, Roilides., *et al.* [23] 65%, Pfaller., *et al*. [24] 66%, Belet N [25] 65.7%, Ariff S [26] 55% of isolation rates in their respective studies. Indian studies which reported almost similar findings were S. Narain [27] 53.3% and Kaur R [28] 50%. However, Kotwal A., *et al*. [29] noted a much higher prevalence of *C.albicans* (78.1%).

However certain other Indian studies showed non albicans Candida species as the most frequently isolated species. S Shivprakashan [30], Goel N [31], Kothavade R J. [32], Deorukhkar SC., *et al*. [33], Deepak Juyal., *et al.* [34] showed *C. tropicalis* as the most frequently isolated species. This species variation may be due to the differences in empiric or prophylaxis practices.

The spectrum of candidiasis varies from country to country. Although *C.albicans* remains the most common isolated spp. from cases of candidemia in USA, Europe, and South America (Brazil), its prevalence is decreasing over the time and non albicans Candida spp. are increasing. The ARTEMIS Surveillance Study which was carried out over a period of 6.5 years (1997–2003) in 127 medical centers in 39 countries has shown an increase in the prevalence of Candida species like *C. tropicalis* (4.6% in 1997 to 7.5% in 2003) and *C. parapsilosis* (4.2% in 1997 to 7.3% in 2003) [35,24]. This particular surveillance study showed a 2 to 10-fold increase in the isolation rates of rare species like *C. guillermondii*, *C. kefyr* and *C. rugosa.*

Although *C. albicans* was the most commonly isolated species (59.2%) in our study non albicans Candida (NAC) also substantially caused candidiasis. The next most common isolate, *C. tropicalis* formed 14.3% of the total isolates. Kontoyiannis., *et al.* [37] and Ariff S [26] also observed *C. tropicalis* as the second most common Candida species after Candida albicans to cause candidiasis. S Narain [27], Gelotar P., *et al.* [38], Kaur R [28] from India reported 23.3%, 36% and 40% of isolation rate of *C. tropicalis* respectively. *C. tropicalis* is becoming an increasingly frequent pathogen in NICU.

C. parapsilosis was the third common species isolated (12.2%). In contrast to our study C. parapsilosis has been reported as the second most common spp. in neonates in many western studies [23,19,25,38].

Kaufmann and Fairchild [3] have found *C. glabrata* as the most common emerging spp. Occurrence of *C. glabrata* sepsis was noted commonly in patients with significant higher gestational age and birth weight compared to sepsis with non glabrata spp. *C. glabrata* was the second most common NAC spp. isolated in the study conducted by Deorukhkar SC., *et al*. [33]. However, we found a much lower incidence of infection by *C. glabrata* (4.1%). According to several investigators, the increase in the frequency of infections has paralleled the increased use of fluconazole in some hospitals. In a more recent study, however, investigators described the association between *C. glabrata* infection and amphotericin B use rather than fluconazole [39].

Other less commonly isolated Candida spp., in order of frequency included *C. guilliermondii* (6.2%), *C. dubliniensis* (2%) and *C. krusei* (2%).

In 39 patients who developed candidiasis, the most commonly associated risk factors were the use of broad spectrum antibiotic therapy (100%), presence of a peripheral catheter (100%), babies born by vaginal delivery (89.7%), low birth weight (76.9%), longer stay in hospital (76.9%). All these factors were found to be significantly associated with the development of neonatal candidiasis ($p < 0.05\%$). Administration of long term broad spectrum antibiotic drugs may precipitate alimentary tract candidiasis by reducing normal bacterial flora which inhibits the growth of fungi [40]. The growth of Candida may be stimulated by the antibiotic itself [41]. In a similar study by Narang., *et al.* [42] and Goel N [31] who found broad spectrum antibiotic therapy (100%), peripheral catheter (100%), LBW (95%) and prematurity (94%) were the most commonly associated risk factors with neonatal candidiasis.

In this study 76.9% neonates & infants with candidemia had LBW which was similar to the findings of Agarwal J., *et al*. [43].

Duration of hospital stay was another major risk factor found to be associated with candidiasis in our study.

These finding were similar to a study done by Kaufman [3], Ariff S [26] and Howell [44].

We also observed that total parenteral nutrition in 46.1% patients with Candida infection was not very commonly associated with candidiasis. Although it is an important risk factor, it was not found to be significantly associated with candidiasis. This finding is in accordance with that of Abi-Said., *et al.* [45] who also found that parenteral nutrition and presence of a peripheral catheter do not significantly increase the risk of candidemia in their study.

Candida albicans was the most common species isolated from the patients who had peripheral catheter, who were on broad spectrum antibiotics (100% in each group), had low birth weight, born vaginally, had respiratory distress, duration of hospitalization greater than 7 days and were preterm. However, there was no significant differences in demographic or risk factors found between neonates and infants infected with C. albicans and those with non albicans Candida (NAC) spp. ($p > 0.05$). Similar observations were made by Roilides., *et al.* [23].

Candida spp. have various virulence factors that facilitate proliferation, they may result in adhesion to the epithelium and invasion of the host tissue. In the present study, we observed that all the isolates (100%) produced hemolysin, 43 isolates (87.8%) showed biofilm formation, 19 isolates (38.8%) showed proteinase production, phospholipase production was formed in 17 (34.7%) and pseudohyphae formation by 10 (20.4%) Candida isolates.

All the virulence markers were significantly associated with the development of candidiasis among neonates and infants. However, among all these factors biofilm and hemolysin production were found to be highly significant ($p < 0.001$). This finding was in accordance with the study done by Shin JH., *et al*. [46]. The presence of significantly associated virulence factors is an indication that most Candida strains were highly virulent.

The susceptibility pattern of Candida isolates shows that 87.8% isolates were susceptible to fluconazole and clotrimazole, 93.9% isolates were susceptible to ketoconazole, 98% to amphotericin B and all the isolates (100%) were susceptible to nystatin and itraconazole. Resistance was observed in 12.2% Candida isolates to fluconazole and clotrimazole, 6.1% isolates to ketoconazole and 2% isolates to amphotericin B. These findings are in agreement with a study conducted Xess., *et al*. [47] who reported 11.7% resistance to fluconazole and Belet N., *et al*. [25] (8.5%). In contrast to our study Narang., *et al*. [42] and Kotwal., *et al.* [29] found a higher rate of fluconazole resistance (24% and 26% respectively).

In this study, we found more resistance to azole group of antifungal agents as compared to amphotericin B in Candida isolates similar to the study by Changdeo S. Aher [48]. Azole resistance in Candida spp. is of concern because these drugs are frequently used as therapeutic alternatives to amphotericin B. Azole group of antifungal agents are preferred because they are easy to administer and are less nephrotoxic.

In this study resistance to fluconazole was observed in 10.3% isolates of *C. albicans*. Similar susceptibility of *C. albicans* isolates was also reported by Mokaddas., *et al*. [49], Fadda., *et al.* [50] and Rizvi M.W., *et al.* [51]. In India, there is a lack of multicentric studies regarding antifungal susceptibility pattern. However, there are few studies from different parts of the country which give some idea regarding the epidemiology of antifungal resistance among candidemia isolates. Recently azole resistance was seen more common in NAC spp. as compared to C. albicans, we also found a higher rate of fluconazole resistance among NAC (15%) as compared to *C. albicans* (10%). Deorukhkar., *et al*. [33] also found a higher drug resistance among NAC isolates. Among *C. tropicalis* 1 (14.2%) and 2 (28.6%) isolates were fluconazole and clotrimazole resistant respectively. Fluconazole resistance was observed in 27.3% of NAC spp. 14.2% of *C. tropicalis* and 100% of *C. dubliniensis* and *C. krusei*. Fluconazole (or Azole) resistance is predominantly the consequence of previous exposure to fluconazole (or other azoles), particularly repeated and long-term exposure [52].

In our study the results of susceptibility by disc diffusion method and with broth microdilution method were found to be almost same. 3.4% isolates of *C. albicans* had MIC value of 32 µg/ ml. 6.9% of *C. albicans* and 16.7% of *C. tropicalis* had a MIC value of > 32 µg/ ml and 100% of *C. dubliniensis* had a MIC value of 64 µg/ ml. This showed that 6.9% isolates of *Candida albicans* were resistant to fluconazole and 1(3.4%) isolate was dose dependent sensitive, while 1(16.7%) isolate of C. tropicalis and 1(100%) isolate of *C. dubliniensis* were resistant

to fluconazole. Pfaller., *et al.* [53] have also reported similar MICs for fluconazole (32 to 128 µg/ ml). Colombo., *et al*. [54] reported MIC value of > 32 µg/ ml for fluconazole. However, they reported a MIC range of 0.125 to > 32 µg/ ml.

Overall 10.2% Candida spp. were resistant to fluconazole by broth micro dilution method which was approximately same as by disc diffusion method (12.2%), as one isolate of *C. albicans* was dose dependent sensitive.

The results of susceptibility pattern of ketoconazole and amphotericin B were found to correlate with the findings of disc diffusion method. We did not find any resistance to itraconazole and nystatin. These findings were in accordance with Pfaller., *et al*. [55].

The incidence of overall mortality in the study population was 41%. A number of studies have shown that *C. albicans* was associated with significantly higher mortality than are another Candida species [56,57].

In the present study mortality was associated with almost all species of Candida and least mortality was associated with *C. parapsilosis*.

In the recent NICHD Neonatal Network survey of VLBW infants, patients with *C. albicans* sepsis had a mortality of 44% compared to 16% for those with *C. parapsilosis sepsis* [57]. This may be related in part to the timing of infection, with vertically transmitted *C. albicans* causing infection earlier, when the immune system is more compromised, and horizontally transmitted *C. parapsilosis* causing infection in an older, more immunocompetent host.

However, higher mortality was seen in children suffering from non albicans Candidiasis (52.9%) as compared to *C. albicans* (31.8%).

Conclusion

Clinicians should strongly suspect Candida infection other than a bacterial infection in neonates and infants belonging to high risk group. Pediatricians should request for fungal culture and antifungal susceptibility testing before initiating antifungal prophylaxis. Non albicans candidiasis should be considered when initiating antifungal prophylaxis as they possess a different antifungal susceptibility spectrum from *C. albicans*.

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