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Original Research Paper

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SPECIES DISTRIBUTION AND ANTIFUNGAL SUSCEPTIBILITY OF BLOOD STREAM *CANDIDA* ISOLATES IN NEONATE AND PEDIATRICS AGE GROUP FROM A TERTIARY CARE HOSPITAL IN NORTH INDIA

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ABSTRACT Candidemia has emerged as the leading cause of invasive mycosis in hospitalized patients with more than seventeen species of *Candida* causing this infection.The study was conducted in Lady Hardinge Medical College, New Delhi for a period of one year and 5 months during November 2012 to March 2014.A total of 200 *Candida* species isolated from blood of neonates and children Overall, *C. tropicalis* (48, 24%) was the most common species isolated followed by *C. krusei* (42, 21%Majority (125, 62.5%) of *Candida* species were isolated from male patients with a male to female ratio of 5:3. Male children dominated in both neonates (74.3%) and non neonates (54.2%) groups

KEYWORDS :

INTRODUCTION

Candidemia has emerged as the leading cause of invasive mycosis in hospitalized patients with more than seventeen species of *Candida* causing this infection. Candidemia is most commonly seen in the immunosuppressed patients with severe neutropenia or in patients with intravenous catheter.[1] Other risk factors predisposing to candidemia are low birth weight and prematurity in neonates, prolonged antibiotic courses, malignancy, human immunodeficiency virus, malnutrition, multiple invasive interventions like central venous catheter, ventilator support and total parental nutrition.[2] Isolation of fungus, identification of organism and antifungal susceptibility testing takes time. Delay in initiation of appropriate antifungal therapy in invasive fungal infections causes increase in risk of mortality and morbidity, duration of hospital stay and also the cost of treatment in critically ill and immunocompromised children.[3,4]

In western countries including USA and European countries *Candida albicans* is still the commonest agent causing candidemia. In Asia especially in India, non albicans *Candida* is emerging as the most common cause of candidemia.[5] A recent multicentric study by Chakrabarti *et al* has shown *C.tropicalis* as the commonest species in Indian ICU setting.[5]Antifungal susceptibility testing is pivotal as many less common species of *Candida* are emerging as opportunistic pathogens, less susceptible to antifungal agents and acquire resistance more easily.[1,2] In addition, certain species of *Candida* are intrinsically resistant to one or more antifungal agents [6]. Identifying the local distribution of *Candida* species may be essential for the emperic treatment especially in the settings where antifungal susceptibility testing is not available.

MATERIAL AND METHOD

The study was conducted in Lady Hardinge Medical College, New Delhi for a period of one year and 5 months during November 2012 to March 2014. The study was approved by the ethical committee of our hospital. A total of 200 *Candida* species isolated from blood of neonates and children with clinical features of sepsis were included in the study. Blood samples were collected in BacT/ALERT 3D (bioMerieux™) paediatric blood culture bottles and incubated for 7 days. Antifungal susceptibility testing was performed for amphotericin B, fluconazole, itraconazole, voriconazole, posaconazole and caspofungin by broth microdilution technique as per CLSI M27-A3 and the results were read after 24 hour of incubation. The antifungal susceptibility was validated using control strains *C. parapsilosis* ATCC 22019 and *C. krusei* ATCC 6258. Antifungal susceptibility testing results were interpreted as per the recommendations of CLSI M27-S3 and M27-S4. Species specific clinical breakpoints for five most common species of *Candida* including *C. albicans*, *C. glabrata*, *C. tropicalis*, *C. krusei*, and *C. parapsilosis* were determined for caspofungin, fluconazole and voriconazole whereas for amphotericin B and posaconazole MIC of >1 ug/ml was considered as resistant. [7]

Clinical details recorded for each patient included the risk factors such as low birth weight, prematurity, prior antibiotic usage, duration of ICU stay, total parental nutrition, central venous catheter insertion, ventilator support, history of surgery, haematological malignancy and immunosuppressive drugs. All patients were divided into two groups as neonates (0 - 28 days) and non-neonates (29 days – 18 years). Data analysis was done with the help of SPSS version 13 software. Qualitative data significance was tested by Chi square test and numerical variable significance was tested by Mcnemar s chi-square test.

RESULTS

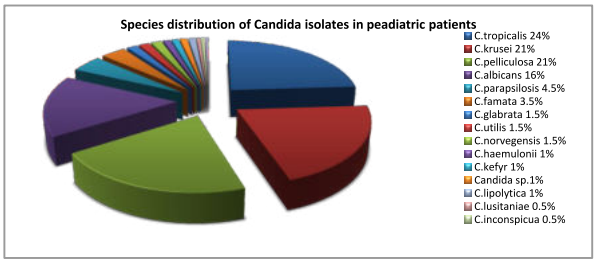

Fig 1: Species distribution of Candida isolated from pediatrics patients

Table 1: Antifungal susceptibility of *Candida* species with different antifungal drugs determined by Microbroth dilution (CLSI M27-A3) [9]

Drugs	Species	MIC Range	S		SDD		I		R	
			n	%	N	%	n	%	n	%
Amphotericin B	Total Candida	0.25-16	168	84	0	0	-		32	16
	C.tropicalis	0.25-2	36	75	0	0	-	-	12	25
	C.krusei	0.25-2	32	76.2	0	0	-	-	10	23.8
	C.pelliculosa	0.25-1	42	100	0	0	-	-	0	0
	C.albicans	0.25-2	26	81.3	0	0	-	-	6	18.8
	Other spp	0.5-16	32	88.9	0	0	-	-	4	11.1
Caspofungin	Total Candida	0.12-1	171	85.5	-	-	27	13.5	2	1
	C.tropicalis	0.12-0.50	39	81.3	-	-	9	18.8	0	0
	C.krusei	0.12-1	33	78.6	-	-	8	19	1	2.4
	C.pelliculosa	0.12-0.50	42	100	-	-	0	0	0	0
	C.albicans	0.12-0.50	24	75	-	-	8	25	0	0
	Other spp	0.12-1	33	91.7	-	-	2	5.6	1	2.8
Fluconazole	Total Candida	0.12-64	170	85	24	12	-	-	6	3
	C.tropicalis	0.12-2	48	100	0	0	-	-	0	0
	C.krusei	0.12-32	0	0	22	52.4	-	-	20	47.6
	C.pelliculosa	0.12-16	41	97.6	1	2.4	-	-	0	0
	C.albicans	0.12-16	31	96.9	0	0	-	-	6	18.8
	Other spp	0.12-64	30	83.3	1	2.8	-	-	5	13.9
Voriconazole	Total Candida	0.03-16	163	81.5	24	12	-	-	13	6.5
	C.tropicalis	0.12-1	33	68.8	12	25	-	-	3	6.3
	C.krusei	0.06-16	37	88.1	2	4.8	-	-	3	7.1
	C.pelliculosa	0.03-0.50	42	100	0	0	-	-	0	0
	C.albicans	0.06-16	31	96.9	0	0	-	-	6	18.8
	Other spp	0.03-0.50	32	88.9	4	11.1	-	-	0	0
Posaconazole	Total Candida	0.03-16	186	93	0	0	-	-	14	7
	C.tropicalis	0.012-0.50	48	100	0	0	-	-	0	0
	C.krusei	0.06-8	39	92.9	0	0	-	-	3	7.1
	C.pelliculosa	0.06-1	42	100	0	0	-	-	0	0
	C.albicans	0.03-16	21	65.6	0	0	-	-	11	34.4
	Other spp	0.03-0.50	36	100	0	0	-	-	0	0
Itraconazole	Total Candida	0.03-16	82	41	101	50.5	-	-	17	8.5
	C.tropicalis	0.12-1	0	0	42	87.5	-	-	6	12.5
	C.krusei	0.06-16	3	7.1	28	66.7	-	-	11	26.2
	C.pelliculosa	0.03-1	32	76	9	21.4	-	-	1	2.8
	C.albicans	0.12-16	3	9.4	22	68.8	-	-	7	27.9
	Other spp	0.06-0.50	18	50	17	42.2	-	-	1	2.8

(S-sensitive, SDD- susceptible dose dependent, I- intermediate, R resistant)

DISCUSSION

Last three decades have witnessed an increase in the prevalence of blood stream infection due to *Candida* spp. It has been reported as the 4th most common cause of BSI in United States.[8] A multicentric study by Chakrabarti *et al* states an overall incidence of 6.51 cases per 1000 admissions.[5] In the present study non albicans *Candida* (84%) were more compared to *C.albicans* (16%) This is comparable to other Indian studies which also show an isolation of 75-85% of non albicans *Candida*.[10]A similar trend has been reported from other countries but the percentage is lower (35-60%) compared to India.[11] The increase is mainly attributed to the increased azole prophylaxis and therapy.[12]

C. tropicalis (24%) was the most common species among the *Candida* isolates from BSI in our paediatric study population. This is similar to other Indian studies.[13] Amphotericin B showed a resistance of 16% in our study. 100% sensitivity was shown by other Indian studies on neonates and adult population also show a higher susceptibility of 92-100 %.Chander J *et al* reported a resistance of 18.5%. [14]Fluconazole resistance was seen in 3% of isolates in our study. Sharma N *et al* [(61)] reported a resistance of 17.8% to fluconazole [13]Our study showed a resistance of 6.5% to voriconazole. 100% sensitivity is reported by most authors while only 56% was reported by Kothari A *et al* [15]Reason for this low sensitivity was not mentioned. Significant association of important risk factors for candidemia in neonates was associated with low birth weight, prematurity, ICU stay and use of central venous catheter. These risk factors have also been observed in other studies. [10,16] In children > 28 days old important risk factors associated were prior antibiotic usage, immunosuppressive drugs and haematological malignancies. Higher antibiotic usage is a major concern. It has been well established by other others also.[17]

CONCLUSION

The epidemiology of candidemia is changing with an upsurge in non albicans *Candida* and increase in resistance to the antifungals. These all factors lead to increased morbidity and mortality. To curtail this problem there is a need for the antibiotic policy to be in place and implemented to reduce the antibiotic usage. Health care practices need to be strengthened with a special attention to infection control practices. There is a need for more multicentric studies in the paediatric population to monitor the trend of species distribution and antifungal susceptibility of *Candida* isolated from this age group of patients so as to lower the morbidity and mortality caused by this entity.

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