Research Article

Invasive candidiasis in Pediatric ICU

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Abstract

Background and objectives: The aim of the present study is to evaluate the conventional methods for the diagnosis of invasive candidiasis in Pediatric Intensive Care Unit (PICU).
Subjects and methods: The study was carried out on 80 critically ill patients who were admitted to Pediatric Intensive Care Unit (PICU) with one or more risk factors for fungal infection were included in the study. Blood Culture was done using Sabaroud dextrose agar (SDA). **Results:** ten cases were positive for fungi by blood cultures out of 80 patients, 8(10%) cases were candida spp., 1 case (1.3%) was aspergillus fumigatus and 1case (1.3%) was kodamaea ohmeri. Among the candida positive cases by blood culture. **Conclusion**: Candida species are the most frequent cause of IFI in PICU
Key Words: IFI, invasive candidiasis, PICU.

Introduction

Candida is the most common cause of opportunistic fungal infections worldwide. Candida is a member of normal flora of skin, mouth, vagina, and stool. It is found in the environment, flowers, water, and soil[9]. Candida includes around 154 species. Among these, six are most frequently isolated in human infections. C. albicans (50% of cases) is the most abundant and significant species, C. tropicalis, C. glabrata, C. parapsilosis, C. krusei, and C. lusitaniae are also isolated as causative agents of Candida infections[12].

The species distribution has changed over the past decades. Whereas Candida albicans had previously been the dominating pathogen, this species today accounts for only half the isolates detected in many surveys[6].

Candida albicans is the most common cause of invasive candidiasis; however, in last decades, with the introduction of antifungal prophylaxis, there has been a reduction in the proportion of invasive candidiasis due to C. albicans, but an increase in cases of IFIs caused by non - albicans Candida spp. such as C. krusei, C. parapsilosis, and C. glabrata amongst others which may vary in virulence and susceptibility to the antifungal drugs commonly used[8].

Invasive candidiasis comprises both candidemia and deep-seated tissue candidiasis. Candidemia is generally considered as the more common type of the disease, and it accounts for the majority of cases included in clinical trials. Deep-seated candidiasis arises from either hematogenous dissemination or direct inoculation of candida species to a sterile site, such as the peritoneal cavity[8].

Subjects and Methods

Study design:

The current study was carried out at Obstetric, Gynecological and Pediatric Hospital, Minia University in the period from June 2016 to September 2017. The study was performed on 80 critically ill patients who were admitted to Pediatric Intensive Care Unit (PICU).They were 40 males and 40 females. Their ages ranged from 1.2 to 70 months with a mean age of 14.7 months.

Patients clinically suspected to have invasive fungal infections such as fever, cough or retrosternal pain; oral mucositis or perianal pain, drug history for antibiotics or corticosteroids, history of chemotherapy, duration of the disease and hospital stay.
In addition to the laboratory investigations; five milliliters venous blood were withdrawn, one ml of venous blood was collected on Egyptian blood culture media (EDM bottles), one ml of venous blood was mixed with EDTA for CBC, three ml of venous blood was left to be clotted in the incubator and centrifuged at 2500 rpm for 10 minutes. Separated serum divided into aliquots and used for assay of urea, creatinine, random blood sugar.

Routine laboratory investigations:
CBC was determined by automated cell counter Sysmex KX-21N (TAO Medical Incorporation, Japan), Renal function tests (urea and creatinine), and Random blood glucose were assayed using fully automated clinical chemistry auto-analyzer system Konelab 60i (Thermo Electron Incorporation, Finland)**.**

Special investigations:
Blood Culture (EDM) bottles were incubated aerobically at 37°C. then subculture was done every week for 4 weeks onto 2 plates of SDA, for primary isolation and propagation of molds and yeast. One plate of SDA was incubated at 37°C and the other was incubated at 25°C. Plates were inspected every other day for fungal growth for the 1st 2 weeks then twice weekly for the next 2 weeks. Also, the blood culture bottle was subcultured on blood agar and Mac Conkey agar (aerobically at 37°C) every 2 days for the 1st week for identification of bacterial growth. Any growth was observed and identified macroscopically according to organism morphology, microscopically according to shape of hypheal element, conidia production, scotch tape preparation (for molds) and budding oval bodies by gram stain (for yeast).

Statistical analysis
Data were coded and entered using the statistical package SPSS version 21. Data was summarized using mean and standard deviation for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Frequencies were compared between the different methods of diagnosis and the risk factors using binary logistic regression. Odds ratio (OR) with 95% confidence intervals was calculated. Comparison of non-parametric quantitative variables was done using Mann Whitney test. Fisher exact test was used for qualitative data between two groups when the expected frequency is less than 5. P value <0.05 was taken as statistically significant.

Among the risk factors for fungal infections; ventilation had the highest percentage (65%), 52 cases out of 80 patients. while corticosteroids intake had the lowest one (1.3%). Other risk factors had variable frequencies as in Table (2).

Among the studied 80 patients, 44 cases did not show microbial growth on blood culture, 26 patients (32%) had bacterial growth with CONs with the highest bacterial frequency (10%), 4 cases (5.1%) had fungal growth with Candida albicans represented 2(2.5%), Aspergillus fumigatus represented (1.3%) and Kodamaea ohmeri was isolated from one case (1.3%). Six cases of the studied patients had mixed bacterial and fungal infections 6/80 (7.8%) where Candida tropicalis 3/80 (3.8%), Candida parapsillosis 1/80 (1.3%) and Candida albicans represent 2/80 (2.5%) AS shown in Table (5). See figures (1&2).

When comparing those with positive blood culture for fungal infections and those who did not, it was found that antibiotic use (>1W), long hospitalization period (> 2W), and high number of risk factors show a significant differences (P<0.01) as shown in table (3). This was confirmed when using simple binary logistic regression analysis as shown in table (4).

Table 2: Risk factors of fungal infections in the studied patients:

Risk factors*	***N (%)***
Ventilation	52(65%)
Central venous line	44(55%)
Antibiotics (>1W)	19(23.8%)
Sepsis	15(18.8%)
Hospitalization (> 2W)	11(13.8%)
DM	5(6.3%)
Neutropenia	4(5%)
TPN	3(3.8%)
Corticosteroids	1(1.3%)

Table 3: Relationship of demographic data and fungal results of blood culture:

		Fungal growth on Blood culture		**P value**
		-Ve (n=70)	**+Ve (n=10)**	
Age *	Range (months) Mean ± SD Median	(1.2-70) 15.4±16.7 10	(3-24) 9.6±8.1 6.5	0.402
Sex $^{\beta}$	Male Female	32(45.7%) 38(54.3%)	8(80%) 2(20%)	0.087
Risk factors $^{\beta}$				
Mechanical ventilation	No Yes	25(35.7%) 45(64.3%)	3(30%) 7(70%)	1
Neutropenia	No Yes	67(95.7%) 3(4.3%)	9(90%) 1(10%)	1
Antibiotics (>1W)	No Yes	59(84.3%) 11(15.7%)	2(20%) 8(80%)	**<0.001***
Central venous line	No Yes	32(45.7%) 38(54.3%)	4(40%) 6(60%)	1
Sepsis	No Yes	57(81.4%) 13(18.6%)	8(80%) 2(20%)	1
TPN	No Yes	67(95.7%) 3(4.3%)	10(100%) 0(0%)	1
Corticosteroids	No Yes	69(98.6%) 1(1.4%)	10(100%) 0(0%)	1
DM	No Yes	66(94.3%) 4(5.7%)	9(90%) 1(10%)	0.497
Hospitalization (> 2W)	No Yes	66(94.3%) 4(5.7%)	3(30%) 7(70%)	**<0.001***
Number of risk factors / patient*	Range Mean ± SD Median	(1-3) 1.7±0.7 2	(2-4) 3.2±0.6 3	**<0.001***

Table 5: Blood culture results of all patients:

Blood culture results [β]	Type	N (%)
-Ve	*No growth*	44 (55%)
Bacterial 26(32.1 %)	*CoNS*	8(10%)
	Klebseilla	6(7.5%)
	E.coli	3(3.8%)
	Acinetobacter	4(5%)
	Pseudomonas	2(2.5%)
	Enterobacter aerogenes	2(2.5%)
	Enterococci	1(1.3%)
Fungal 4(5.1%)	*Candida albicans*	2(2.5%)
	Aspergillus fumigatus	1(1.3%)
	Kodamaea ohmeri	1(1.3%)
Mixed infection 6(7.8%)	*Candida albicans + CoNS*	1(1.3%)
	Candida albicans + Klebseilla	1(1.3%)
	Candida tropicalis + E. coli	1(1.3%)
	Candida tropicalis + S.aureus	1(1.3%)
	Candida tropicalis + Pseudomonas	1(1.3%)
	Candida parapsillosis + E. coli	1(1.3%)

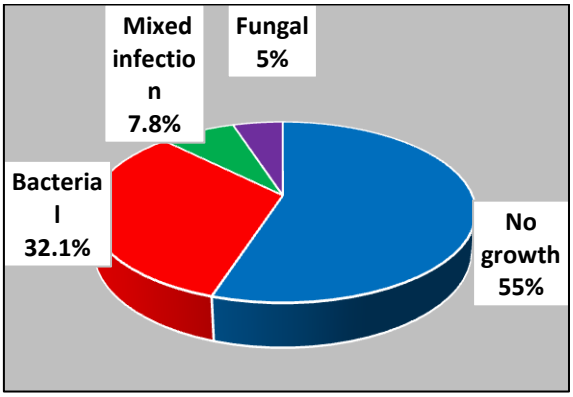

Figure 1: blood culture results for patients with suspected fungal infection
N.B: mixed infection=bacterial and fungal

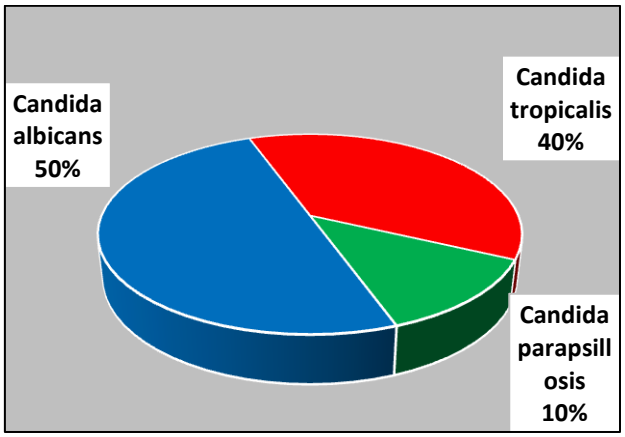

Figure 2: percentages of different candida species isolated from blood culture for patients with suspected fungal infection

Discussion

Invasive candidiasis is the most common fungal disease among hospitalized patients in the developed world. Invasive candidiasis comprises both candidemia and deep-seated tissue candidiasis [8].

Our results showed that 10 cases were positive for fungi by blood cultures out of 80 patients, 8(10%) cases were candida spp., 1 case (1.3%) was aspergillus fumigatus and 1case (1.3%) was kodamaea ohmeri .

Our results were comparable with the low detection rate of Moraco and coworkers 1999 [10] who found that only 4/90 (5.5%) of their studied patients with hematological malignancies had positive blood cultures for fungi. Also, Badiee and colleagues 2008[4] who studied the microbiologic data of 310 immunosuppressed patients at Nemazi hospital, southern Iran, found that 33/310 (10.6%) of their studied patients had positive blood cultures for fungi. In addition, Yumiko et al., 2013[15] did not report a single positive IFI by blood culture among high risk patients with hematological disorders admitted to the cancer center of Mie University Hospital in Japan.In contrast, Azab et al., 2015[3] reported a higher frequency of IFI in 79 immunosuppressed patients with hematological disorders admitted to Zagazig University Hospitals as he reported 24.1%.

The variable frequencies of different Candida spp. could be explained by the fact that most pathogens were fastidious organisms or poorly growing fungi as a result of prior antifungal use or rapid clearance of Candidemia at the time the blood sample is collected [13].

In our study C.tropicalis was the most prevalent NCAC species 3/8(37.5%), followed by C.parapsilosis was1/8 (12.5%). These results were in broad accordance with Awasthi et al., 2011 [2] who reported higher percent of C. tropicalis that represented (71.5%) of candidaemia cases, also concomitant with Almeida et al., 2013[1] having C. tropicalis as the most common (42%).

In contrast to, Dutta and Palazzi 2011[7] who reported that among the NCAC group, C.parapsilosis was the most common (23.9%), followed by C. tropicalis (14.8%), also, Bruder-Nascimento et al., 2010[5] where C. parapsillosis had the highest percentage (48%) and Yapar, 2014[14] showing C. parapsillosis and C. tropicalis (23.9%) and (16.8%) respectively in a study made in Argentina.

The variable frequencies of different Candida species explained by Pfaller and Diekema 2004[11] who reported that, this may be affected by the geographic area, underlying diseases, antifungal treatment, differences in patient populations and infection control policies.

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