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ORIGINAL ARTICLE

The prevalence of pediatric nosocomial fungal infections

Parisa Badiee*, Hadis Jafarian

Professor Alborzi Clinical Microbiology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

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ABSTRACT

Background and Objectives: The aim of this study was to identify the incidence of nosocomial fungal infections in pediatric patients and evaluate the etiological agents, risk factors, and sites of infections.

Materials and Methods: Clinical samples were cultured to assess fungal colonization. When fungal nosocomial infections were suspected according to the European Organization for Research and Treatment of Cancer criteria, clinical samples were evaluated using direct microscopic, culture, and molecular methods. Susceptibility patterns of the isolates were evaluated according to the Clinical and Laboratory Standard Institute.

Results: From the 1450 patients, 190 cases (5.5%) were evaluated for nosocomial fungal infections. *Candida* colonization was observed in 35 (18.4%) patients. The rate of nosocomial fungal infections in pediatrics was 2.69% (12 cases with proven and 27 cases with probable infections, 39/1450). Bloodstream and lungs were the frequent infected sites of patients' body. *Aspergillus* species (*Aspergillus flavus* and *Aspergillus fumigatus*), *Candida* species (*Candida albicans*, *Candida parapsilosis*, *Candida glabrata*) and Mucorales were the etiologic agents of infections. Caspofungin and luliconazole were effective antifungal agents for isolated fungi. The rate of mortality in infected patients suffering from proven and probable infections was 15.4% (6/39 cases).

Conclusion: Due to the high mortality rates of fungal infections in pediatrics, it is essential to identify modifiable risk factors, and implement control measures along with early detection techniques in pediatric populations.

Keywords: Pediatrics; Fungal drug resistance; Colonization; Fungal infection; *Candida*; *Aspergillus*

INTRODUCTION

Pediatric fungal nosocomial infections are observed in children who have received medical and healthcare facilities after one week of hospitalization. These infections are not present or incubated during admission, but are acquired during hospitalization. Pediatric patients with immune deficiency, such as hematopoietic stem cells or solid organ transplantation, are more susceptible to infections (1, 2). The risk of developing fungal nosocomial infections is high in patients who have been hospitalized for a long time, and those who have received immunosuppressive drugs and antibiotic medications for a long time (1, 2). In a study by Zingg et al., of 392 microorganisms isolated from pediatric and adult patients (770 cases), 28 (7%) were fungi, including *Aspergillus* and *Candida* species (3). In a retrospective study involving children under 12 years of age, 35 invasive fungal infections were detected per 1000 hospitalized patients. These infections were most prevalent (77.7%) in infants less than one year old. The mortality rate associated with these infections was 36% (4).

The most prevalent etiologic agents were *Asper-*

*Corresponding author: Parisa Badiee, Ph.D, Professor Alborzi Clinical Microbiology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran. Tel: +98-71-36474304 Fax: +98-71-36474303 Email: badieep@gmail.com

gillus species, *Candida* species, and Mucorales (5). *Aspergillus* species are filamentous fungi commonly and live in the surrounding environment and are a significant cause of invasive pulmonary aspergillosis in immunocompromised patients. *Candida* is a yeast-like fungus that is part of the natural human flora but can present as etiologic agent of infection in immunocompromised patients, and those with indwelling catheters. *Mucor* is a non-septate filamentous fungi that causes rare but severe infections that can affect the sinuses, brain, lungs, and other organs.

Symptoms of the disease vary depending on the organ involved (6). Common signs and symptoms include fever, malaise, chills, cough, chest pain, respiratory distress, diarrhea, vomiting, abdominal pain, and skin rash. Patients may develop sepsis, shock, organ failure, and death in severe cases (6). Radiological imaging is indispensable for the identification of pediatric fungal nosocomial infections. Chest X-rays may show infiltrates, consolidations, nodules, or cavities in pulmonary aspergillosis. Computerized tomography scans may reveal halo or crescent signs, cavity signs in the lung, sinusitis, or brain abscesses (7, 8).

The incidence of fungal disease in patients can lead to prolonged hospitalization, high costs of treatment, and death. The aim of this study was to retrospectively identify the occurrence of nosocomial fungal infections in pediatric patients and evaluate the etiologic agent, risk factors, and sites of infection.

MATERIALS AND METHODS

Study population and demographic data. This was a cross-sectional, single-center study at Nemazi Hospital in Shiraz, Iran, a 1000-bed tertiary care university Hospital, including pediatrics internal, surgery, infectious disease, neurosurgery pediatric department, and intensive special care units. Admitted patients without signs and symptoms of infectious disease during the 10-month (April 2019 to January 2020) study period were entered in this prospective study. In total 3446 patients were admitted during the study period. Inclusion criteria were patients with non-febrile and no having symptoms for infection at time of hospitalization and the hospitalization period needed to be more than 6 days. This study was accepted by the research committee of Alborzi Clinical Microbiology Research Center. If the hospitalization period of the patients were more than 6 days, oral and rectal swabs, urine, and sputum (if possible) were cultivated on Sabouraud-dextrose agar (Merck, Darmstadt, Germany) to evaluate fungal colonization. Information regarding age, gender, and clinical and radiological findings of the patients was collected.

Isolation and identification. All tests were performed under a Class II biosafety cabinet and Lab technologists wore respirators, gloves, and eye protection. A fungal nosocomial infection was confirmed when the patient showed symptoms of infection and the fungus was isolated from the patient's clinical specimen seven days after admission to the hospital (9). Whenever the attending physician suspects nosocomial fungal infections, according to the published criteria (7, 8, 10), other clinical samples such as midstream urine, wound swab, sputum, bronchoalveolar lavage, cerebrospinal fluid (CSF), pleural fluid, and tissue biopsy were examined microscopically using the 10% KOH and cultured on sabouraud dextrose agar with chloramphenicol. The patients' blood samples were cultured by BACTEC (Becton–Dickinson, Sparks, MD, USA). *Aspergillus* species were identified according to colony morphology and lactophenol cotton blue direct smear. API-20 C AUX system (BioMerieux, St. Louis, MO, USA) was used to identify isolated *Candida* spp.

PCR study. *Aspergillus* and *Candida* systemic infections were identified by Real-time PCR. 200 microliters of clinical samples were used to extract DNA with QIAmp DNA Minikit (Qiagen, Hilden, Germany) by the manufacturer's recommendations. The methods for identification of *Candida* DNA was designed by Shin et al. (11). Primers and TaqMan probes for identification of *Aspergillus* species were used according to Kami et al. (12). TaqMan probes and primers used in this project were manufactured by Metabion (Martinsried, Germany). To prevent contamination, all samples were tested in a laminar flow cabinet and under sterile conditions.

Antifungal susceptibility testing. Antifungal susceptibility tests of the mold to seven antifungal agents including amphotericin B (AMB), caspofungin (CAS), voriconazole (VOR), luliconazole (LUL), itraconazole (ITR), posaconazole (POS), and isavuconazole (ISA), (Sigma, UK) were assessed according to Clinical and Laboratory Standard Insti-

tute (CLSI) M38 and M61 documents (13, 14). The powders of the mentioned antifungals were obtained from Sigma and dissolved in DMSO (Merck, Germany) (for AMB, FLU, VOR, ITR, POS, LUL, and ISA) or water (for CAS). Molds were grown on potato dextrose agar (Merck, Germany) for 3-7 days. A standard suspension of conidia was prepared for each in RPMI 1640 broth (Sigma Aldrich, USA) buffered with MOPS [3-(N-morpholino) propanesulfonic acid] (Sigma, Germany) at a final concentration of 0.165 mol/L at pH 7.0. The minimum inhibitory concentration (MIC) and the minimum effective concentration (MEC) for each antifungal were defined as international criteria (14).

For yeast isolates, a susceptibility test was done based on CLSI M27, M59, and M60 documents (15, 16). The final concentration of the antifungal agents for CAS, AMB, POS, ITR, and VOR was 8 to 0.016 µg/mL; FLU 0.064-32 µg/mL; LUL and ISA 4 to 0.008 µg/mL. All yeast isolates were sub-cultured twice onto potato dextrose agar. A suspension of isolated yeast was made in sterile water and the cell density was adjusted by a spectrophotometer to achieve 0.5 McFarland turbidity at 530 nm wavelength. The quality controls for the antifungal sensitivity test were *C. krusei* ATCC 6258 and *C. parapsilosis* ATCC 22019.

Definition of fungal infection. Improving clinical studies relies on the essential elements of accuracy and uniformity to explain fungal infections. The original European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) Consensus Group have defined criteria and classified fungal infections as possible, probable, and proven (8). In the present study, clinical, radiological, and mycological criteria in patients were evaluated for fungal infection and patients were categorized based on their specific conditions (8).

Statistical analysis. Data were collected by Statistical Package for the Social Sciences (SPSS) version 16. Statistical analysis was performed. The analysis of fungal species distribution and susceptibility to antifungal drugs were evaluated using descriptive analysis. To find the relationship between variables, the Chi-square Test was used and a p-value <0.05 was considered as significant.

RESULTS

In the study period, 3446 patients were hospitalized to pediatric wards (medical, surgical, and ICU) (Fig. 1). The mean stay period in the wards was 5.04 days (range 2-57 days). Among these, 1450 cases (non-febrile and no positive findings for infection on admission time) were entered into the study. According to the definition of nosocomial fungal infection, host factor, clinical, radiological, and mycological evidence of patients, 190 cases hospitalized for more than six days were evaluated for nosocomial fungal infections. Of the patients included in the analysis, 84/190 (44.2%) were female and the mean age was 6.6 years (Table 1). Antifungal drugs were prescribed as prophylaxis for 91 (47.9%) patients. *Candida* colonization was observed in 35 (18.4%) patients: seven (3.6%) in urine, six (3.2%) in sputum, eight (4.2%) in mouth, and six (3.2%) in rectum. Eight patients were colonized in more than one site. *Candida albicans*, *C. krusei*, and *C. glabrata*, were the most colonized species isolated from patients.

Twelve patients were diagnosed with proven invasive fungal infections. Fungi were isolated from the CSF in two, the abdomen in one, the sinus biopsy in two, and the blood samples in three patients. Fungal infections were confirmed in three patients according to a pathologic study of patients' biopsies (Table 2). In proven cases, the etiologic agents in 33.3% of patients were yeasts (*C. albicans* and *C. glabrata*) and in 66.7% of patients they were molds (*Aspergillus* species and *Mucorales*). Twenty-seven patients were classified as probable cases with clinical, radiological, and mycological criteria (Table 3). We examined 380 blood and 56 other clinical samples (CSF, abdominal fluid, sputum) for *Aspergillus* spp. and *C. albicans* infections (872 PCR assays). According to the patient's signs and symptoms, 151 cases were classified as possible IFI. The rate of fungal infections in proven and probable pediatric wards was 2.69% (39/1450). In the ICU wards, this rate was significantly higher ($p<0.05$). The more frequent sites of fungal infection were the bloodstream, lung, and gastrointestinal tract. The most prevalent risk factors were hematologic disorders, transplantation, and prolonged ICU stay.

From patients' clinical samples, 56 fungi species were isolated. The isolates included *C. albicans* (32, 57.1%), *C. glabrata* (15, 26.8%), *C. parapsilosis* (4, 7.1%), *A. fumigatus* (2, 3.6%), *A. flavus* (2, 3.6%) (3, 5.46%). Mucorales species were identified by mi-

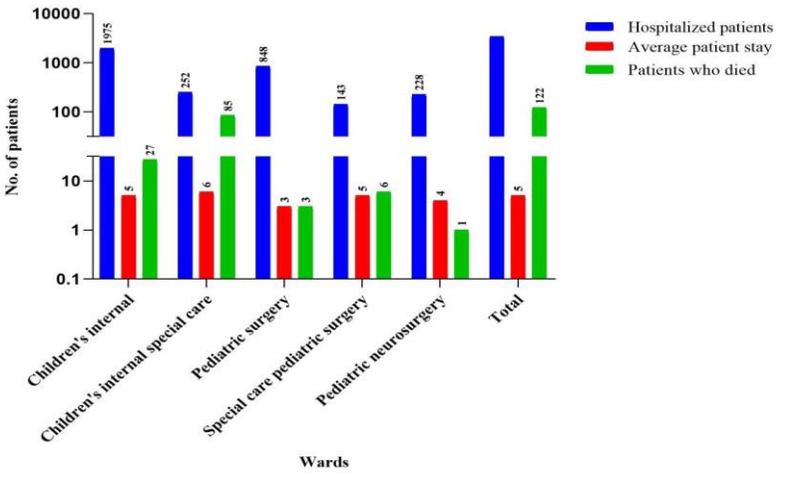

Fig. 1. Information about patients admitted in different pediatric wards during study period

Table 1. Demographic criteria of pediatric patients

Characteristics		Number (%)
Sex	Male	106 (55.8%)
	Female	84 (44.2%)
Age	Minimum	1 month
	Maximum	17 years
	Mean	6.6 years
	Standard deviation	5.3 years
Background	Hematologic disorders	36
	Transplant	48
	Immunodeficiency patient	19
	Car accident	6
	Febrile neutropenia	11
	Infection disease	54
	Others	16
Colonization	Without colonization	155 (81.6%)
	Colonized:	35 (18.4)
	Oral lesion	8 (4.2%)
	Anus	6 (3.2%)
	Sputum	6 (3.2%)
	Urine	7 (3.6%)
	More than one sit	8 (4.2%)
Antifungal	Not used	99 (52.1%)
therapy	Used	91 (47.9%)
EORTC criteria	Proven	12 cases (6.3%)
	Probable	27 cases (14.2%)
Etiologic agents	*Candida albicans*	2 cases
in proven cases	*Candida glabrata*	2 cases
	Aspergillus flavus	2 cases
	Aspergillus fumigatus	2 cases
	Fusarium species	1 cases
	Mucorales	3 cases
Outcome	Alive	184 (96.8%)
	Died	6 (3.2%)

croscopic examination. The antifungal susceptibility information for isolated species is presented in (Tables 4 and 5). MIC90 values of antifungals against *C. albicans* species were 0.064 µg/mL for CAS and VOR; 0.5 µg/mL for AMB and LUL, 0.5 µg/mL for ISA; 4 µg/mL for ITR, 1 µg/mL for POS; and 8 µg/mL for FLU. In terms of *C. glabrata*, the MIC90 values of VRC, FLU, ITR, POS, LUL, and ISA were 0.125, 8, 4, 2, 0.25, and 0.5 µg/mL, respectively. The geometric mean values for *C. parapsilosis* for AMB, CAS, FLU, VOR, ITR, POS, LUL, and ISA were 0.032, 0.25,1.414, 0.023, 0.176, 0.063, 0.25, and 0.011 µg/mL, respectively. Among mold isolates, the *Fusarium* species was less sensitive to antifungal agents and POS was more active against this fungus. Caspofungin, LUL, ITR, and ISA were effective antifungal agents for *Aspergillus* isolates. The mortality rate for all pediatric patients during the study periods was 3.5% (122/3446), but in patients with fungal infection (proven and probable) it was 15.4% (6/39 cases).

DISCUSSION

Nosocomial fungal infections have a high mortality rate in children, which is why they are important. They are becoming increasingly prevalent worldwide. In this study mold infections were prevalent fungal infections in infected cases. Invasive pulmonary aspergillosis is more common in children who have compromised immune system (17, 18). The prevalent risk factors were underlying diseases such as hematologic disorders, transplantation, and using antibiotics and central venous catheters (Tables 2 and 3).

Table 2. Patient characteristics of proven fungal infections *

Number	Sex	Age (year)	Host factors	Mycollogical Criteria	Outcome
1	Male	0.5	Acute lymphoblastic leukemia	Isolation of *Candida albicans* from blood culture	Survived
2	Male	6.5	Liver transplant	Diagnosis of fungal infection (Zygomycosis) in liver biopsy	Survived
3	Female	13	Acute lymphoblastic leukemia	Diagnosis of fungal infection (Zygomycosis) in sinuses biopsy	Survived
4	Male	15	Acute lymphoblastic leukemia	Diagnosis of fungal infection (Zygomycosis) in sinuses biopsy	Survived
5	Male	2	Liver transplant	Isolation of *Candida glabrata* from blood culture	Survived
6	Male	10	Aplastic anemia	Isolation of *Aspergillus flavus* from sinuses biopsy culture	Survived
7	Male	14	Liver transplant	Isolation of *Aspergillus flavus* from sinuses biopsy culture	Survived
8	Male	7	Hydrocephaly with shunt	Isolation of *Candida glabrata* from CSF culture	Survived
9	Male	5	hepatoblastoma	Isolation of *Fusarium* species from blood culture	Survived
10	Male	4	Hydrocephaly with shunt	Isolation of *Candida albicans* from CSF culture	Survived
11	Female	15	Prolong ICU stay	Isolation of *Aspergillus fumigatus* in sinuses biopsy culture and positive *Aspergillus* PCR in serum	Survived
12	Male	1	Liver transplant	Isolation of *Aspergillus fumigatus* from abdominal tap	Died

*All admitted patient presented many clinical and radiological signs and symptoms

Candida infections can lead to severe clinical outcomes, including sepsis and death. Early diagnosis of candidiasis is essential since its morbidity and mortality rate is high in hospitalized children. This rate in pediatric patients with invasive candidiasis has been reported to be 7.7-26% in different studies (19-21). The most common causes of fungal disease in pediatrics are *C. albicans* and non-*albicans* such as *C. tropicalis, C. glabrata, C. parapsilosis,* and *C. krusei* (22). Obeed and co-workers in Basrah Province Hospital reported that the most prevalent etiological agents of hospital-acquired infections were *Candida* spp. including *C. albicans, C. parapsilosis, C. glabrata*, and *C. tropicalis* (23). Badiee and co-workers reported that the most prevalent *Candida* spp. isolated from immunocompromised pediatric patients was *C. albicans,* followed by *C. glabrata, C. tropicalis, C. famata, C. kefyr,* and *C. kuresi* (24). Also, the predominant isolated *Candida* strains were reported as *C. albicans* and *C. glabrata* in ICU wards in Iran (25). The data extracted from the present study is similar to other studies. The prevalence rates of fungal infections are different according to the hospital setting, patient population, and etiological agent.

Invasive *Aspergillus* infections is a serious risk to the health of children admitted to hospitals worldwide due to their immunocompromised conditions and prolonged healthcare stays. Although there have been many advances in the diagnosis and treatment of fungal diseases, invasive aspergillosis can lead to high morbidity and mortality rates ranging from 52.5%-85% in children with cancer, and 45%-80% of the pediatric patients who have undergone allogeneic hematopoietic stem cell transplantation in different studies (26-29). Zaoutis et al. in a multicenter study reported that the mortality rate in 666 children with invasive aspergillosis was as high as 85% (30). A

Table 3. Patient characteristics of probable fungal infections

Number	Sex	Age (year)	Host factors	Mycological criteria	Outcome
1	Female	1	Prolong ICU stay	Positive *Aspergillus* PCR in serum*	Survived
2	Male	1	Leukocyte adhesion deficiency	Positive *Aspergillus* PCR in serum	Survived
3	Male	14	Ewiding sarcoma	Positive *Aspergillus* PCR in serum	Survived
4	Male	1.5	Liver transplant	Positive *Aspergillus* and *Candida albicans* PCR in serum	Survived
5	Male	3	Prolong ICU stay	Isolation of *Aspergillus fumigatus* from sputum	Died
6	Female	1	Severe Combined Immunodeficiency	Positive *Aspergillus* and *Candida albicans* PCR in serum	Died
7	Male	11	Acute lymphoblastic leukemia	Positive *Aspergillus* PCR in serum	Died
8	Male	4	Prolong ICU stay	Positive *Aspergillus* PCR in serum	Survived
9	Male	12	Fanconi anemia	Positive *Aspergillus* PCR in serum	Survived
10	Male	6	Bone marrow transplant	Positive *Aspergillus* PCR in serum	Survived
11	Female	1	Prolong ICU stay	Positive *Aspergillus* PCR in serum	Survived
12	Male	6	Acute lymphoblastic leukemia	Isolation of *Aspergillus flavus* from sputum	Survived
13	Male	1.5	Liver transplant	Positive *Aspergillus* PCR in serum	Died
14	Female	10	Liver transplant	Positive *Aspergillus* PCR in serum	Survived
15	Female	6	Liver transplant	Positive *Aspergillus* PCR in serum	Survived
16	Male	7	Non-Hodgkin's lymphoma	Isolation of *Aspergillus flavus* from sputum	Survived
17	Female	8	Liver transplant	Positive *Aspergillus* PCR in serum	Survived
18	Male	4	Acute lymphoblastic leukemia	Positive *Aspergillus* PCR in serum	Survived
19	Female	5	Liver transplant	Isolation of *Fusarium* species from sputum	Survived
20	Male	3	Liver transplant	Isolation of *Aspergillus flavus* from sputum	Survived
21	Male	9	Liver transplant	Isolation o*f Aspergillus flavus* from sputum	Survived
22	Male	15	Neurogenic bladder	Isolation of > 10^5 *Candida* species from urine and Positive *Candida albicans* in serum	Survived
23	Male	2	Liver transplant	Positive *Aspergillus* and *Candida albicans* PCR in serum	Survived
24	Male	2.5	Liver transplant	Positive *Aspergillus* PCR in serum	Died
25	Female	7	Prolong ICU stay	Positive *Aspergillus* PCR in serum and CSF	Survived
26	Female	1	Prolong ICU stay	Isolation of *Aspergillus fumigatus* from sinus aspirate	Survived
27	Male	4	Prolong hospital stay due to SIADH**	Isolation of *Aspergillus flavus* from sputum	Survived

All admitted patient presented many clinical and radiological signs and symptoms

* In two consecutive PCR test

**Syndrome of inappropriate antidiuretic hormone secretion

study managed at a hospital in Iran reported that the incidence rate of probable/proven aspergillosis in the pediatric patients admitted at the hematology/oncology wards was found to be 27.4% (one proven and 9 probable) (31). *Aspergillus* species in the current study were identified as the etiologic agents of proven (4/12, 33.3%) and probable (25/27, 92.6%) nosocomial fungal infections.

The incidence of mucormycosis in pediatric patients is rare but it has been increasing in recent years. The mortality rate between 33 to 67% has been reported for this infection based on the infection site, underlying condition, and the antifungal administered (32). Identification of the etiologic agents is available by means of culture, direct microscopic and histopathological examination of the samples, and molecular

Table 4. Minimum inhibition ı oncentration (MIC, µg/ l) range, MIC_{50}, MIC_{90}, ε nd MIC_{GM} di ributions of the eight antifungals, according CLSI protocol

Candida species	Antifungal agents	Range (µg/ml)	MIC_{50} (µg/ml)	MIC_{90} (µg/ml)	MIC_{GM} (µg/ml)
Candida albicans	Amphotericin B	0.016-3	0.125	0.5	0.141
(32 isolates)	Caspofungin	0.016-0.25	0.016	0.064	0.027
	Fluconazole	0.25-8	0.5	8	0.801
	Voriconazole	0.016-0.064	0.016	0.064	0.025
	Itraconazole	0.064-4	0.125	4	0.359
	Posaconazole	0.016-1	0.25	1	0.213
	Luliconazole	0.008-1	0.25	0.5	0.210
	Isavuconazole	0.008-1	0.016	0.25	0.028
Candida glabrata	Amphotericin B	0.016-1	0.5	1	0.309
(15 isolates)	Caspofungin	0.016-0.064	0.064	0.064	0.028
	Fluconazole	4-8	4	8	4.604
	Voriconazole	0.064-0.125	0.064	0.125	0.083
	Itraconazole	2-4	2	4	2.828
	Posaconazole	0.5-2	2	2	1.320
	Luliconazole	0.008-0.25	0.064	0.25	0.135
	Isavuconazole	0.125-0.5	0.125	0.5	0.164
Candida parapsilosis	Amphotericin B	0.64-2	0.064	1	0.032
(4 isolates)	Caspofungin	0.25	0.25	0.25	0.250
	Fluconazole	1-2	1	2	1.414
	Voriconazole	0.016-0.032	0.016	0.032	0.023
	Itraconazole	0.125-0.25	0.125	0.25	0.176
	Posaconazole	0.032-0.25	0.032	0.25	0.063
	Luliconazole	0.25	0.25	0.25	0.250
	Isavuconazole	0.008-0.016	0.008	0.016	0.011

Table 5. In vitro susceptibility patterns of mold species isolates to seven antifungal agents

	Antifungal	Range (µg/ml)	MIC_{GM} (µg/ml)	Mean MIC (µg/ml)
Mold species (2 *Aspergillus flavus*,	Amphotericin	0.5-2	0.757	0.900
2 *Aspergillus fumigatus*, 1 *Fusarium*	Caspofungin	0.016-8	0.063	1.616
spp.)	Voriconazole	0.125-4	0.870	1.675
	Itraconazole	0.016-0.25	0.055	0.091
	Posaconazole	0.032-8	1.154	3.006
	Luliconazole	0.008-8	0.218	1.726
	Isavuconazole	0.25-5	0.435	0.450

tests (33). Also, magnetic resonance imaging (MRI) can characterize the rhino-orbital and cerebral infections (34). Hematological malignancy is the most underlying disease of mucormycosis in children, but other risk factors such as uncontrolled diabetes, bone marrow, solid organ transplantation, and aggressive immunosuppressive therapy have been reported as well. Paranasal sinus or sino-orbital is the most common sites of infection in pediatrics. Infection may present in the skin, lungs, and gastrointestinal tract (32, 33). In the present study, three cases of proven mucormycosis were reported in liver transplant re-

cipients and two patients with acute lymphoblastic leukemia (Table 2). The site of infection in one case was the liver, and in two, the sinuses (Table 2).

In this study, fluconazole didn't present efficacy against *C. albicans* and *C. glabrata* (MIC_{90} 8 μg/ml). Voriconazole, CAS, ISA, and LUL were effective for all *Candida* isolates. Antifungal susceptibility patterns in mold isolates differed according to the etiologic agents and antifungal drugs. The susceptibility patterns of the *Candida* spp. in this study were similar to other studies (34, 35). Voriconazole was effective against *A. flavus* species and less active against *A. fumigatus* and *Fusarium* species.

Prevention and control measures are essential in decreasing the prevalence of pediatric nosocomial fungal infections. To achieve this goal, strict hand hygiene, environmental cleaning and disinfection, isolation precautions, appropriate use of antimicrobial agents, and early removal of indwelling devices should be considered. Immunocompromised patients should be managed in a specialized unit with strict infection control measures.

This study had limitations. The study population was limited to one hospital. Also, in some patients, before sampling, treatment with antifungal drugs was started as prophylaxis, which can have an effect on culture results. Also, *C. albicans* has a sufficient number of isolates, thus the antifungal susceptibility tests may not accurately reflect the patterns of resistance in the other fungal etiologic agents. Our suggestion is to conduct future studies in multiple hospitals with larger populations.

CONCLUSION

Pediatric fungal infections pose a considerable threat to the health and mortality rates of children admitted to hospitals worldwide because of their immunocompromised conditions and prolonged healthcare stays. According to our data, *Aspergillus*, *Candida*, and *Mucorales* are the etiological agents of nosocomial fungal infections in immunocompromised pediatric patients (hematologic disorders, transplantation, and long stay in ICU wards). Infection is present in the lungs, sinuses, and blood (febrile neutropenia). Therefore, it is essential to identify the etiologic agents, their susceptibility to antifungal agents, and risk factors, along with early detection techniques, such as molecular-based methods, that aid in the timely handling of nosocomial fungal infections in pediatric populations.

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