

Oropharyngeal candidiasis in children with lymphohematopoietic malignancies in Mashhad, Iran

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Abstract

Background and Purpose: Over the past years, the role of fungi as a cause of nosocomial infections in hospitalized patients has been accentuated. *Candida* species constitute an important group of fungi causing diseases in immunocompromised patients. Oropharyngeal candidiasis continues to be a prevalent infection in immunodeficient patients. In this study, we aimed to determine the incidence of oropharyngeal candidiasis in children with lymphohematopoietic malignancies.

Materials and Methods: In total, 102 patients with lymphohematopoietic malignancies and 50 healthy controls were examined in terms of *Candida* infections via direct sampling of the oropharyngeal cavity. Fresh smears were prepared with 10% potassium hydroxide and Gram staining was carried out. Subsequently, the obtained specimens were cultured on Sabouraud dextrose agar for further analysis.

Results: The most common *Candida* species were *Candida albicans* (31%), other non-*C. albicans* species (14.7%), *C. glabrata* (6.8%), and *C. krusei* (0.98%) in the case group, while in the control group, other non-*C. albicans* species (10%) and *C. albicans* (8%) were the most common species.

Conclusion: In the present study, *Candida* species were the most common fungal pathogens in pediatric cancer patients; therefore, efforts should be made to prevent fungemia and fungal pneumonia. Also, non-*C. albicans* species must be considered as a new risk factor for pediatric cancer patients.

Keywords: *Candida*, Hematopoietic Malignancies, Oral candidiasis

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Introduction

Over the past years, the role of fungi as a cause of nosocomial infections in hospitalized patients has been accentuated [1]. These fungi are a major cause of morbidity and mortality, given the increased length of hospital stay [2, 3].

Oropharyngeal candidiasis, which is caused by *Candida* species through the involvement of hard and soft palates, tongue, buccal mucosa, and floor of the mouth, is a very common problem of the mucosal membranes of oropharynx. Although in the majority of patients, this infection is caused by *Candida albicans* as a commensal organism [1, 4-6], it may be also caused by other *Candida* species, such as *C. glabrata*, *C. tropicalis*, and *C. krusei* [1, 7].

The prevalence of oropharyngeal candidiasis

continues to be high in immunocompromised patients [8-10]. In many cases, clinicians dealing with immunocompromised and critically ill patients have shown a link between *Candida* colonization and subsequent infections [11, 12]. Colonization of *Candida* species occurs in up to 80% of critically ill patients receiving intensive care.

Despite the recent advances in microbiological techniques, primary diagnosis of invasive candidiasis remains challenging, resulting in the delayed detection of candidiasis [12]. Accurate identification of *Candida* strains is highly important, considering the ability of these strains to cause infections and induce susceptibility to antifungal agents. Compared to *C. albicans*, the importance of non-*C. albicans*

species such as *C. glabrata* and *C. krusei* has been more recognized due to their improved resistance to certain antifungal agents [13].

Physiologic differences between pediatric and adult patients alter susceptibility to infections caused by different *Candida* species [3]. Therefore, the aim of the present study was to evaluate the incidence of oropharyngeal candidiasis and compare the causative agents among children with lymphohematopoietic malignancies and healthy controls.

Material and Methods

This cross-sectional study was conducted in the hematology-oncology ward of Dr Sheikh Children's Hospital, affiliated to Mashhad University of Medical Sciences and Parasitology and Mycology Laboratory of Imam Reza Hospital in July 2009-2010. In this study, three methods including direct smear, staining, and culture were used for laboratory investigation of *Candida* infections.

In total, 102 patients with lymphohematopoietic malignancies and 50 healthy individuals (control group) at the nurseries of Qaem and Imam Reza hospitals were examined for *Candida* infections via direct sampling of the oropharyngeal cavity, fresh smear with 10% potassium hydroxide (KOH), and direct microscopic examination with Gram staining of each sample. Subsequently, the samples were inoculated into Sabouraud dextrose agar (SDA, Himedia Laboratories, Mumbai, India), and positive cultures were transferred to CHROMagar *Candida* medium (HiMedia Laboratories, Mumbai, India) for further analysis.

Results

This study was conducted among 102 patients with lymphohematopoietic malignancies (mean age: 7 years) and 50 healthy children (mean age: 4.5 years) as the control group. In the case and control groups, the most prevalent age range was 3-6 years, accounting for 30% and 50% of the subjects in the case and control groups, respectively. Overall, 66% and 33% of the subjects in the case group were male and female, while 56% and 44% were male and female in the control group, respectively.

Among 102 patients with lymphohematopoietic malignancies, acute lymphoblastic leukemia was the most common underlying hematological malignancy (83.3%), followed by lymphoma (6.8%), acute myeloblastic leukemia (3.9%), non-Hodgkin's lymphoma (3.9%), and sarcoma (1.9%). It should be mentioned that all the patients had received chemotherapy.

In the case group, positive results were reported in 37% and 56% of the subjects in direct smear and culture, respectively, while in the control group, positive results were reported in 8% and 24% of the participants in direct smear and culture studies, respectively. Therefore, culture studies showed sensitivity and specificity of 51% and 92%, respectively.

Among patients with lymphohematopoietic malignancies, 54% had clinical signs including white spots on the mouth and tongue (30%), redness of the mouth (14%), lip fissures (12%), burning mouth (10%), sore throat (7%), and fissure of tongue (5%). On the other hand, 22% of the subjects showed no clinical signs or symptoms; however, in the control group, no signs or symptoms of candidiasis were reported in the oral cavity.

The most common *Candida* species on CHROMagar *Candida* were *C. albicans* (31%), other non-*C. albicans* species (14.7%), *C. glabrata* (6.8%), and *C. krusei* (0.98%) in the case group, while in the control group, the most common species was other non-*C. albicans* species (10%), followed by *C. albicans* (8%) (Table 1).

Discussion

Fungal organisms are a cause of nosocomial infections and a major source of morbidity and mortality. Modern medicine is faced with great challenges, considering the increased length of hospital stay and high healthcare costs in critically ill or immunocompromised children and patients with nosocomial infections, hematological diseases, or other malignancies [3, 14-18].

In studies by Kumar et al. in Chennai, India and Walsh et al. in France, invasive fungal

Table 1. *Candida* species isolated from the case and control groups

Culture	Case group		Control group		Total	
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
<i>C. albicans</i>	32	31.3	4	8.0	32	21.05
<i>C. glabrata</i>	7	6.8	0	0.0	7	4.6
Unknown yeasts	3	2.9	3	6.0	6	3.9
Other non- <i>C. albicans</i> species	15	14.7	5	10.0	24	15.7
<i>C. krusei</i>	1	0.98	0	0.0	1	0.65
Negative	44	43.1	38	76.0	82	53.9

infections such as aspergillosis and candidiasis were introduced as important causes of morbidity and mortality in immunocompromised children, particularly those with hematologic malignancies, stem cell transplantation, and acquired immunodeficiency [14, 19].

The prevalence of fungal infections is increased by the rise in the number of immunocompromised patients, chemotherapy dose intensity, increased length of hospital stay, extensive ulceration of mucous membranes, prolonged treatment with multiple broad-spectrum antibiotics, and common use of indwelling intravascular devices [11, 15, 20].

Based on a study by Saha et al., the ascribable mortality of acute candidiasis is 10-15% in children suspected of septicemia [21]. The present study was performed to evaluate the incidence of oropharyngeal candidiasis and to compare the type of causative fungi in children with lymphohematopoietic malignancies and control subjects.

In this study, the most common *Candida* species were *C. albicans* (31%), other non-*C. albicans* species (14.7%), *C. glabrata* (6.8%), and *C. krusei* (0.98%) in the case group, respectively. In the control group, the most common species were other non-*C. albicans* species (10%) and *C. albicans* (8%), respectively. *C. albicans* has been long recognized as the most common cause of disseminated candidiasis, followed by *C. glabrata* and other non-*C. albicans* species in pediatric and adult patients [11, 14, 20, 22].

Another aspect of candidemia is the economic burden on the patient and hospital. This economic impact has been associated with the increased costs of care including the use of antifungal agents and prolonged length of

hospital stay, especially in severely immunosuppressed patients with hematological malignancies [20, 23-26].

Conclusion

C. albicans, other non-*C. albicans* species, and *C. glabrata* were the most common *Candida* species among the evaluated patients. *Candida* species were the most common fungal pathogens in pediatric cancer patients. Therefore, efforts should be made to prevent fungemia and fungal pneumonia. Also, non-*C. albicans* species must be considered as a new risk factor for pediatric cancer patients.

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Authors' Contributions

F.B., N.Z., and Z.B. designed and supervised the research. F.B. and Z.AA. edited the final manuscript, and Soraya Kakhi and M.G. performed the tests.

Conflicts of interest

The authors declare no conflicts of interest regarding the publication of this paper.

Financial disclosure

The authors declare no financial interests related to the materials of the study.

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