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SHORT COMMUNICATION

The microbiology, epidemiology, risk factors, and clinical therapy of candidemia in burn patients hospitalized in Velayat Teaching Hospital, Rasht, northern Iran

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ABSTRACT

Background and Objectives: The study aimed to investigate the epidemiology and clinical therapy of candidemia in burn patients hospitalized in Velayat Hospital, Rasht, Iran.
Materials and Methods: The blood samples of suspected patients were cultured and PCR-sequencing was performed. Antifungal susceptibility testing was done by the CLSI M27-A4 document.
Results: Four blood samples were identified as positive. *Candida parapsilosis* complex (3 out of 4, 75%) was the predominant leading cause of candidemia. MIC values showed that all isolates were susceptible to itraconazole, amphotericin B, and 5-flucytosine.
Conclusion: It seems necessary to pay attention to *Candida* non-*albicans* species in antifungal therapy.

Keywords: Candidemia; Burns; Epidemiology; Microbiology; Microbial sensitivity tests

INTRODUCTION

Burn is one of the most common types of traumatic injuries with high morbidity and mortality rates (1). Damaged skin caused by burn, bacterial and fungal overgrowth in the intestine after burn injury, and the skin and mucosal normal flora of the patient could be potential sources responsible for various infections (2).

Although bacterial microorganisms play the main part in infecting burn patients, fungal species can also be detected in many patients with burn complications (3). The global incidence of infections caused by yeasts and molds in patients with burn injuries has changed from 6.3% to 40% in the last 10 years (4). Infection with *Candida* spp. is the most common fungal infection, which accounts for nearly 80% of nosocomial fungal infections (5). Candidemia (a bloodstream infection caused by yeasts in the genus *Candida*) is often caused by *Candida albicans*, al-

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though, recently, an increasing number of infections have been associated with other *Candida* species which are more resistant to azoles and have created a public health concern (6). Azole resistance in *Candida tropicalis* and *Candida parapsilosis,* and echinocandin resistance in *Candida krusei* have revealed the importance of precise and rapid identification of pathogens and determining antimicrobial resistance patterns for a better treatment (7, 8).

Until now, no research has been done on the identification of the causative agents of candidemia in burn patients hospitalized in Guilan province, therefore, the present research aimed to investigate the epidemiology, risk factors, and clinical therapy of candidemia in thesepatients.

MATERIALS AND METHODS

This study was carried out from December 2021 to March 2023 in Velayat Teaching Hospital, the only burn center of Guilan province, Iran.

All participants had at least one of the clinical criterion for candidemia listed below, either at the time of study entry or within four days before the study entry.

• Fever (feeling warm to the touch all over the body and/or an oral/tympanic temperature ≥ 100.4°F (38.0°C), and/or rectal temperature ≥101.4°F (38.6°C), and/or an axillary temperature ≥ 99.4°F (37.4°C)) for more than 96 hours, without response to broad-spectrum antibiotic treatments,

• Patients with severe second-degree or third-degree burns,

• Patients staying in the ICUs or surgical units for more than 10 days, or receiving Total Parenteral Nutrition (TPN), or patients who were performed totally implantable venous port catheter, or intubated patients, or patients who had undergone extensive surgeries,

• Patients with signs or symptoms of candidemia/ invasive candidiasis, which may include the following: feeding intolerance with increased gastric residuals, occult or gross bloody stools, distended stomach, color change, persistent and severe thrombocytopenia, lethargy, hyperglycemia, hypotension, glycosuria, and unexplained metabolic acidosis.

• To prevent false-negative results, patients who had taken any systemic antifungal agents before enrollment were excluded from the study.

Blood samples (approximately 20 mL for each patient) were collected. Brain heart infusion biphasic medium bottles (Merck, Darmstadt, Germany) were utilized to culture blood samples. The blood culture bottles were incubated at 37°C for 21 days. Any growth of *Candida* species in blood cultures was considered as evidence of candidemia.

Yeast isolates were identified based on chlamydoconidia production in cornmeal agar (Becton, France) and colony color on chromogenic CHROMagar Candida medium (CHROMagar, Paris, France). Furthermore, for confirmation of diagnosis, all isolates were subjected to PCR and sequencing techniques. The Clinical and Laboratory Standards Institute document M27-A4 (CLSI M27-A4) broth microdilution protocol was used as a guideline for testing antifungal susceptibility of yeasts (9). Susceptibility of the isolates to fluconazole (Sigma Chemical Co, St Louis, Mo), amphotericin B (Bristol-Myers SP, Dublin, Ireland), 5-fluorocytosine (Sigma Chemical Co), itraconazole (Janssen-Cilag, High Wycombe, UK), voriconazole (Pfizer Inc., New York, NY), and caspofungin (Merck Sharp &Dohme, Whitehouse Station, NJ) were tested. This study was approved by ethical committee of Guilan University of Medical Sciences (the number of Ethics Committee protocol: IR.GUMS.REC.1400.477).

RESULTS

In the present study, 200 blood specimens were taken from 200 burn patients (including 149 males and 51 females) hospitalized in Velayat Teaching Hospital who also had criteria for candidemia. The age range of patients was 1.5 to 84 years with a mean ± SD of 41.09 ± 24.32 years. Of those, 4 (2%) patients with candidemia were diagnosed. The mean age of burn patients with candidemia was 53.00 ± 18.68 years (age range of 48 to 61 years). The overall incidence of candidemia was higher in females than in males (rate ratio 3:1).

One-half (2 of 4, 50%) of the patients had diabetes mellitus and hypertension as underlying conditions.

According to the results of mycological and molecular methods, *C. parapsilosis* complex (3 out of 4, 75%) was the predominant leading cause of candidemia followed by *C. tropicalis* (1 out of 4, 25 %).

Antifungal susceptibility test Table 1 showed that, itraconazole (MIC: 0.03 μg/mL), amphotericin B

Table 1. *In vitro* antifungal susceptibility pattern of *Candida* isolates recovered from blood cultures of 4 burn patients with candidemia hospitalized in Velayat Teaching Hospital, Rasht, northern Iran

Strains	Antifungals	MIC range	CLSI M27-A4 Breakpoints (n)		
			R	SDD/I	S
C. papapsilosis complex	AMB	0.06-1.0	-	-	3
(n=3)	FLZ	0.06-4	-	1	2
	ITZ	0.03	-	-	3
	5FC	0.5-2	-	-	3
	VOR	0.012-0.5	-	1	2
	CAS	0.5-8	2	-	1
C. tropicalis	AMB	0.5	-	-	1
(n=1)	FLZ	1.0	1	-	-
	ITZ	0.03	-	-	1
	5FC	1.0	-	-	1
	VOR	0.03	-	-	1
	CAS	0.06	-	-	1

MIC: Minimum inhibitory concentration; R: resistant; SDD: susceptible-dependent-dose; I: intermediate; S: susceptible; AMB: Amphotericin B; FLZ: Fluconazole; ITZ: itraconazole; 5FC: 5-fluorocytosine; VOR: voriconazole; CAS: caspofung

(MIC range: 0.06-1.0 µg/mL), and 5-fluorocytosine (MIC range: 0.5-2.0 µg/mL) were the most active drugs against all *Candida* isolates and no resistance to these antifungal agents was observed. Although, two isolates of *C. parapsilosis* complex were caspofungin-resistant (MIC: 1 µg/mL) and the sensitivity of 33.3% of them to fluconazole (MIC: 4 µg/mL) and voriconazole (MIC: 0.5 µg/mL) was intermediate. Furthermore, the isolated *C. tropicalis* was susceptible to all tested antifungals except for fluconazole, and was classified as fluconazole-resistant (MIC: 1 µg/mL).

DISCUSSION

In the current study, the prevalence of candidemia in burn patients was estimated to be 2%. In a previous study conducted on patients with severe immunodeficiency disorders in Isfahan, Iran the prevalence of candidemia was 1.2% (10). In the present study, *C. parapsilosis* complex was the most prevalent species isolated from blood samples. This is in accordance with the results of studies conducted by González et al., in Mexico (11), Cortés et al., and in Colombia (12). The increasing prevalence of non-*albicans* species is a concern because these species have different patterns of drug resistance that cause challenges in treatment (7).

CONCLUSION

C. parapsilosis complex was the most common *Candida* species causing candidemia in our survey, and *C. parapsilosis* isolates were resistant to caspofungin and susceptible-dose dependent to voriconazole, and fluconazole. This can represent a regional phenomenon and points to the value of careful selection of empiric therapy.

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