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Short Communication

Predominance of *Candida glabrata* in candidemia among patients with solid tumor cancer in Oman: A retrospective study

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ABSTRACT

Objectives: *Candida* species frequently cause bloodstream infections; however, there is a lack of epidemiological studies on candidemia in Oman.

Methods: To address this, we conducted a retrospective study at Sultan Qaboos Comprehensive Cancer and Research Center from October 2021 to October 2023.

Results: Our study identified 27 episodes of candidemia among 26 patients with cancer, with an incidence of 4.9 per 1000 admissions. Non-*albicans Candida* (NAC) prevailed over *C. albicans* (70.37% vs 29.62%), with *C. glabrata* as the predominant NAC species (n = 10; 37%). The 30-day mortality rate was 40.7%, showing no significant difference between NAC and *C. albicans* but was notably higher in critically ill patients ($P = 0.03$).

Conclusion: In Oman, NAC surpasses *C. albicans* as a causative pathogen for candidemia with a high mortality rate.

Brief report

Candida species stand as the fourth leading cause of bloodstream infections [1]. The increase in the incidence of candidemia is linked to factors such as an increasing population of immunocompromised individuals, heightened use of intravascular catheters, a surge in complicated surgical procedures, widespread antimicrobial use, and advancements in diagnostic microbiology [1]. Candidemia poses a significant mortality risk, reaching rates of up to 50%, and places a substantial economic burden [1,2]. Although *C. albicans* remains the most identified causative species, a global shift toward non-*albicans Candida* (NAC) is evident, reflecting trends in various Arab nations [2–4]. However, there is a notable lack of data regarding the epidemiology of *Candida* infections in Oman.

This study aimed to identify predominant *Candida* species, assess antifungal resistance, and uncover outcomes and risk factors for mortality in patients with cancer with candidemia. Our study included patients with cancer, aged 18 years and older, who were admitted with candidemia to the Sultan Qaboos Comprehensive Cancer and Research Center in Muscat, Oman over a 2-year period. Recurrent cases within a 14-day period were excluded. Candidemia diagnosis was confirmed by at least one positive blood culture yielding *Candida* species growth. Central line bloodstream infections were defined as per National Health-

care Surveillance Network criteria. Data on demographics, oncology history, risk factors, *Candida* speciation, antifungal susceptibility, and outcomes were retrospectively extracted from the electronic health care system. Blood cultures were processed using the BACT/ALERT system (bioMérieux SA, France). *Candida* speciation and susceptibility was identified by the VITEK 2 system. Antifungal susceptibility followed the Clinical and Laboratory Standards Institute guidelines.

The incidence rate of candidemia was calculated per 1000 patient admissions, with the 95% confidence interval estimated using the Wald method. Categorical data were summarized using frequencies and percentages and compared using Fisher's exact test. Continuous data were presented as medians with interquartile ranges. The study was approved by the institutional review board at Sultan Qaboos Comprehensive Cancer and Research Center (CCRC-37-2022).

Of the 5469 recorded admissions, 27 cases of candidemia were identified in 26 patients, resulting in an incidence rate of 4.9 per 1000 patient admissions (95% confidence interval 3.4-7.2). The median age of patients diagnosed with candidemia was 58 years (interquartile range 41-67), with 21 (77.8%) episodes occurring in female patients. The *C. glabrata* complex (10, 37%) was the most prevalent, followed by *C. albicans* (8, 29.6%), *C. tropicalis* (3, 11.1%), *C. parapsilosis* (2, 7.4%), *C. krusei* (2, 7.4%), *C. kefyr* (1, 3.7%), and *C. dubliniensis* (1, 3.7%). Among

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Table 1
Baseline characteristics and outcomes of the candidemia episodes (N = 27).

Characteristics	Median	Interquartile range
Age	58	41-67
Female	N	%
	21	77.8%
Malignancy		
Gastrointestinal	7	25.9%
Sarcoma	7	25.9%
Breast	5	18.5%
Biliary	4	14.8%
Gyne-oncology	3	11.1%
Head and Neck	1	3.7%
Clinical characteristics		
Neutropenia	1	3.7%
Total parenteral nutrition	14	51.9%
Central venous catheter	26	96.3%
Antibiotic use within 30 days	24	88.9%
Antifungal use within 30 days	6	22.2%
Abdominal surgery within 30 days	9	33.3%
Source of infection		
Gastrointestinal translocation	7	18.5%
CLABSI	17	63.0%
SSTI	1	3.7%
Urine	1	3.7%
Unknown	1	3.7%
Candida species		
<i>C. albicans</i>	8	29.6%
<i>C. glabrata</i>	10	37.0%
<i>C. tropicalis</i>	3	11.1%
<i>C. krusei</i>	2	7.4%
<i>C. parapsilosis</i>	2	7.4%
<i>C. dubliniensis</i>	1	3.7%
<i>C. kefyr</i>	1	3.7%

SSTI: skin and soft tissue infection; CLABSI: Central line-associated bloodstream infections.

the 26 patients with candidemia, line-related infections (n = 17, 63%) were the predominant source, followed by intra-abdominal infections (5, 18.5%) and biliary infections (2, 7.4%). Other cases were attributed to unknown or complicated urinary tract infections. The key associated risk factors included the presence of a central line (26 of 27; 96%) and a history of antimicrobial exposure (24 of 27; 89%). Detailed patient characteristics are summarized in Table 1.

Antifungal susceptibility testing was conducted for 26 of 27 species. For *C. albicans*, *C. tropicalis*, and *C. parapsilosis*, the antifungals tested included fluconazole, amphotericin B, micafungin, caspofungin, and voriconazole. For *C. krusei* and *C. glabrata* complex, the tested antifungals were voriconazole, amphotericin B, caspofungin, and micafungin. For *C. dubliniensis* and *C. kefyr*, only voriconazole and amphotericin B were tested.

The analysis showed that all *C. albicans* and *C. tropicalis* isolates were pan-susceptible, including fluconazole. Similarly, all other NAC isolates were highly susceptible to voriconazole (100%), amphotericin B (100%), and micafungin (100%). However, among the *C. glabrata* isolates, one was intermediate and the other was resistant to caspofungin. Also, one *C. krusei* isolate was intermediate to caspofungin.

Echinocandins were initiated in all patients, except one who passed away before the blood culture turned positive. Surveillance of blood cultures was conducted for 25 patients. Transesophageal blood cultures were performed in a quarter of the patients (7, 25.9%), all of which were negative for endocarditis. Ophthalmic examination was not done on any of our patients because none of them had ophthalmic symptoms. Step-down to azole therapy was implemented in nine of 25 (36%) patients. Specifically, eight patients were switched to fluconazole, and one patient was shifted to voriconazole. In patients with *C. glabrata*, patients were kept on anidulafungin.

Table 2 summarizes the key elements of candidemia management among our patients. The 30-day crude mortality rate was 40.7%. The

Table 2
Management of candidemia.

Management	N (%)
Species identification	27 (100%)
Echocardiology	7 (25.9%)
Ophthalmic examination	0 (0%)
Empiric therapy	
Anidulafungin	25 (92.6%)
Targeted therapy	9 (36%)
Fluconazole	8(89%)
Voriconazole	1(11%)
Antifungal for at least 14 days after first negative culture	20 (76.9%)
Central venous catheter removal	22 (81.5%)

univariate analysis showed that only intensive care unit (ICU) stay was a significant risk factor for 30-day mortality ($P = 0.02$). NAC species were not found to be associated with an increased risk of mortality ($P = 0.68$).

Despite the significant morbidity and mortality of candidemia, no previous studies have been reported in Oman. This report presents a retrospective analysis of adult patients with cancer at a tertiary cancer center in Muscat, Oman, focusing on the epidemiology of candidemia, *Candida* species prevalence, antifungal susceptibility, and outcomes. Over a 2-year span, the candidemia incidence rate was recorded at 4.9 per 1000 patient with cancer admissions, consistent with findings in similar populations [5].

Our study aligns with global trends showing an increase in NAC species incidence, with 70.4% of episodes attributed to NAC species [2,6]. Recent reports from Arab countries also confirm the predominance of NAC species, emphasizing a diversity in predominant strains [5]. In our study, *C. glabrata* was the most common causative agent of candidemia. This was similar to the findings from Lebanon but contrasts with studies from Kuwait and Saudi Arabia, which reported the predominance of *C. tropicalis* and *C. parapsilosis*, with *C. glabrata* representing only 3-15% [3,4,7]. Notably, Oman has only reported case reports and series detailing *Candida*-associated COVID-19 infections [8]. Regarding antifungal susceptibility, *C. albicans* is considered susceptible to fluconazole, with variation in reported susceptibility rates ranging from 38% to 96% [6,7]. In our study, all eight patients with *C. albicans* isolates demonstrated susceptibility to fluconazole. Among NAC species, *C. glabrata* and *C. krusei* isolates displayed high susceptibility to amphotericin B and micafungin, with fluconazole susceptibility not assessed. The 30-day crude mortality rate in our study was 40.7%, aligning with global observations [2,3]. The identified risk factors for mortality included septic shock, a low European Quality (EQUAL) candida score, ICU stay, and acute kidney injury [2]. In our study, the univariate analysis showed that only ICU stay exhibited a statistically significant association with increased mortality ($P = 0.02$).

The guidelines advocate for echinocandins as a first-line treatment for candidemia, coupled with optimal source control measures, such as central line bloodstream infections [9]. In our cohort, echinocandins were used as the first-line treatment. The need for fundoscopic evaluation and optimal antifungal therapy duration remains debated, with none of our patients exhibiting ophthalmic symptoms warranting fundoscopic evaluation. This practice is supported by the evidence from the American Academy of ophthalmology that recommends against universal funduscopy screening for patients with candidemia [10]. In fact, Infectious Diseases Society of America recommendation for funduscopy is based on low-level evidence [9]. Based on that, we recommended screening for only symptomatic or persistently positive blood cultures. Finally, randomized clinical trials are needed to elucidate the indications of funduscopy in patients with candidemia.

Our study has limitations, including its monocentric, small sample and retrospective design. Nevertheless, it provides crucial insights into candidemia epidemiology and antifungal resistance in Oman, identify-

ing *C. glabrata* as the most prevalent species. The observed 40.7% mortality rate aligns with expectations.

Author contribution

B.A. and J.A. contributed to the review of the literature, conceptualization of the study design, and collection of the data. H.S. contributed to checking and analyzing the data. B.A. contributed to writing the first draft of the manuscript. A.Z., A.G., B.I., M.M., and K.B. contributed to reviewing and visualization of the manuscript. All authors approved the final version of the manuscript.

Declarations of Competing Interest

The authors have no competing interests to declare.

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Ethical approval

Ethical approval was granted by the Institutional review board at the Sultan Qaboos Comprehensive Cancer and Research Center, under authorization number (CCCRC-37-2022).

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