Variability in the clinical distributions of Candida species and the emergence of azole-resistant non-Candida albicans species in public hospitals in the Midwest region of Brazil


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Abstract

Introduction: Incidence and antifungal susceptibility of Candida spp. from two teaching public hospitals are described. Methods: The minimum inhibitory concentrations of fluconazole, voriconazole, itraconazole, and amphotericin B were determined using Clinical Laboratory Standard Institute broth microdilution and genomic differentiation using PCR. Results: Of 221 Candida isolates, 50.2% were obtained from intensive care unit patients; 71.5% were recovered from urine and 9.1% from bloodstream samples. Candida parapsilosis sensu stricto was the most common candidemia agent. Conclusions: We observed variations in Candida species distribution in hospitals in the same geographic region and documented the emergence of non-C. albicans species resistant to azoles.

Keywords: Candidiasis. Candidemia. Epidemiology.
For differentiation between Candida albicans and Candida dubliniensis isolates, duplex PCR was performed as described by Ahmad et al. The primers used were CALF: TGGTATTGCTGTTGGATTGT; S1R: CAGACTCGACATCTTCTCAAT.

The C. glabrata complex was differentiated by using PCRm in accordance with the study published by Romeo et al. The primers used were S1F: GTTGATGCTGTTGGATTGT; S1R: CAATGCCAAATCTCCCAA.

During the study period, 10,680 and 8,542 patients were hospitalized in UH-MAP and UH-FUGD, respectively. A total of 221 Candida species were evaluated. Of these, 164 were isolated from patients admitted to UH-MAP while 57 were isolated from those admitted to UH-FUGD. These represent rates of 15.35 and 6.67 per 1,000 admissions in UH-MAP and UH-FUGD, respectively. The incidence of candidemia in UH-MAP was 1.40 per 1,000 hospital admissions (20, 11.7%). In UH-FUGD, the incidence was 0.58 per 1,000 admissions [5 (8.6%)]. Of the patients admitted to UH-MAP and UH-FUGD, 1,035 (9.7%) were hospitalized in intensive care units (ICUs) [111 (50.2%)]. Elderly patients, as observed in our study, are at high risk of fungal infections due to the reduced immunity and increased incidence rates observed between the two hospitals may be related to the higher number of critically ill patients admitted to UH-MAP compared to UH-FUGD.

The increased incidence of fungal infections observed in recent years has been associated with the increased use of invasive devices, transplantation, and extensive surgeries, among other medical procedures. In our study, the difference in incidence rates observed between the two hospitals may be related to the higher number of critically ill patients admitted to UH-MAP compared to UH-FUGD.

Of the 221 Candida isolates, 78 (35.3%) were C. albicans and 143 (64.7%) were NCA, including 58 (35.4%) C. albicans and 106 (64.6%) NCA species from UH-MAP and 20 (35.1%) C. albicans and 37 (64.9%) NCA from UH-FUGD.

Candida spp. were isolated from 11 different clinical specimens (Table 1), mainly urine [158 (71%)], blood samples [20 (9.1%)], and tracheal aspirate [20 (9.1%)].
TABLE 2: Susceptibility to antifungals of Candida species according to hospitals.

<table>
<thead>
<tr>
<th>Antifungal</th>
<th>MIC range</th>
<th>MIC50/90*</th>
<th>Number by category</th>
<th>MIC range</th>
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<th>Number by category</th>
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</table>

UH-MAP: University Hospital Maria Aparecida Pedrossian; UH-FUGD: University Hospital of the Federal University of Grande Dourados; MIC: minimum inhibitory concentration as defined by Clinical Laboratory Standard Institute; S: susceptible; SDD: susceptible dose dependent; R: resistant; C.: Candida; FLU: fluconazole; VOR: voriconazole; ITRA: itraconazole; AMB: amphotericin B. *MIC50 and *MIC90: MIC at which 50% and 90% of the isolates were inhibited. **Candida glabrata does not have breakpoints for voriconazole because the data were insufficient to demonstrate the in vitro correlation with the clinic. *** Candida krusei was intrinsically resistant in vivo to fluconazole, independent of the minimum inhibitory concentration.
Despite being tertiary and teaching hospitals located in the same region, the two hospitals showed differences in the incidence of Candida infection-causing species (Table 1).

In UH-MAP, the main agent of candiduria was C. albicans [47 (39.5%)], whereas in UH-FUGD, it was C. tropicalis [15 (38.5%)]. The presence of Candida spp. in the urine may indicate infection or colonization of the urinary tract. In hospitalized patients, the detection of Candida as a colonizing agent has clinical relevance because, in immunocompromised patients, it may be a risk factor for candidemia.

Unlike previous studies that reported C. albicans as the main species of candidemia in Latina American medical centers, our study showed that NCA species were most commonly isolated from blood cultures [19 (95%)].

Candida parapsilosis sensu stricto was the main cause of candidemia in UH-MAP [6 (40%)]. In UH-FUGD, no difference was observed in the number of species isolated from blood culture. In a recent review C. parapsilosis sensu stricto was identified as the main NCA species causing candidemia in 25 of 40 studies. In six studies, this species was more prevalent than C. albicans, similar to the observation in the present study. Candida parapsilosis complex is an important agent of candidemia due to their ability to form biofilms and adhere to plastic surfaces such as central venous catheters that are frequently used in critically ill patients.

Previous studies indicate that Candida isolates of various species were susceptible to amphotericin B. In contrast, 132 (57.6%) Candida spp. isolates had decreased susceptibility to azole drugs. Of these, 40 (17.5%) and 11 (17.5%) isolates were considered susceptible dose-dependent (SDD) and resistant to fluconazole, respectively. Regarding itraconazole, 53 (23.1%) isolates were considered SDD while 13 (5.7%) were resistant; finally, 12 (5.2%) isolates were SDD and resistant to voriconazole, respectively. The results of in vitro assessment of the susceptibility to antifungal drugs according to Candida species are shown in Table 2.

Comparing the data for the ICU and non-ICU, there were differences in the distribution of Candida species causing candiduria and candidemia in tertiary teaching hospitals within the same region. We also documented the emergence ofazole drug resistance, mainly in NCA species.

Ethical considerations

Descriptive statistics were used to characterize the variables. The study was approved by the Research Ethics Committee of the Federal University of Mato Grosso do Sul, under the registration number CAAE: 30746214.3.0000.0021

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Conflict of interest

The authors declare that there is no conflict of interest.

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