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Emergence of non-*albicans Candida* species and antifungal resistance in intensive care unit patients

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ABSTRACT

Objective: To evaluate the epidemiology of candidiasis and the antifungal susceptibility profile of *Candida* species isolated from the intensive care unit (ICU) patients.

Methods: The study used a qualitative descriptive design. Relevant samples depending on organ system involvement from 100 ICU patients were collected and processed. Identification and speciation of the isolates was conducted by the biochemical tests. Antifungal susceptibility testing was carried out as per CLSI-M27-A3 document.

Results: Ninety *Candida* isolates were isolated from the different clinical samples: urine (43.3%), tracheal aspirate (31.1%), urinary catheter (12.2%), endotracheal tube (7.8%), abdominal drains (3.3%), sputum (2.2%). The incidence of candidiasis caused by non-*albicans Candida* (NAC) species (63.3%) was higher than *Candida albicans* (36.7%). The various NAC species were isolated as: *Candida tropicalis* (41.1%), *Candida glabrata* (10%), *Candida parapsilosis* (6.7%), *Candida krusei* (3.3%) and *Candida kefyr* (2.2%). The overall isolation rate of *Candida* species from samples was 53.3%. Antifungal susceptibility indicated that 37.8% and 7.8% of the *Candida* isolates were resistant to fluconazole and amphotericin B, respectively.

Conclusions: Predominance of NAC species in ICU patients along with the increasing resistance being recorded to fluconazole which has a major bearing on the morbidity and management of these patients and needs to be further worked upon.

1. Introduction

Nosocomial infections constitute a serious public health problem and are among the major causes of morbidity and mortality leading to increased hospitalization time and consequently, generating high costs for patient treatment [1]. In the recent years, the incidence of nosocomial candidiasis has increased throughout the world, starting from tertiary care centers and spreading to community hospitals [2]. The epidemiological surveillance program in the United States has shown that 5%–10% of patients who admitted in the hospitals acquire nosocomial infection. Of these, about 80% of fungal infections were caused by *Candida* species. According to studies by Centers for Disease Control, *Candida albicans* (*C. albicans*) is the sixth most common cause of nosocomial infections [1].

The frequent use of broad-spectrum antibiotics, central venous catheters, urinary catheters, prosthetic devices and abdominal surgery in intensive care unit (ICU) patients requiring emergency care [3], put patients at a high risk of infection with *Candida* species [4]. Furthermore, ICU admission itself has

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The study protocol was performed according to the Helsinki declaration and approved by the Institutional Ethics Committee of Maulana Azad Medical College & Associated Hospitals, New Delhi, India. Informed written consent was obtained from the patients/guardians.

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become an independent risk factor for the development of *Candida* species infection [5]. The most common species implicated was *C. albicans* recently, when the incidence of non-*albicans Candida* species (NAC) has risen dramatically [6]. In recent decades, several countries around the world have witnessed a change in the epidemiology of *Candida* infections, characterized by a progressive shift from a predominance of *C. albicans* to NAC species [7].

A worrisome trend is the increasing number of reports of fluconazole resistance among species that are typically fluconazole-susceptible, such as *C. albicans*. There are several reports regarding this phenomenon, but larger epidemiologic studies have failed to show a definite geographic or temporal trend toward fluconazole resistance, despite of heavy azoles usage. This epidemiologic shift has greatly impacted the therapeutic choices for initial and definite therapy for this disease [8]. Since there is scanty data on candidiasis in North India, the main objective of present study was to perform a study on the epidemiology of candidiasis and evaluate the antifungal susceptibility profile of the *Candida* species isolated from the ICU patients at our tertiary care hospital.

2. Materials and methods

2.1. Design and setting

A prospective study was focused on epidemiology of candidiasis in ICU patients and to evaluate the antifungal susceptibility profile of *Candida* species isolated from the ICU patients. Relevant samples depending on organ system involvement were collected from the ICU patients of a 1 500 bedded tertiary care hospital and processed in the Department of Microbiology in an Indian medical college.

2.2. Ethics approval

Ethics committee approval was granted by the Institutional Ethics Committee of the College & Associated Hospitals, India. Written consent was taken from the patients and they were informed that their participation was voluntary and that they withdraw from the study at any stage without incurring any penalty.

2.3. Participants

All hospitalized medical/post-operative patients admitted to ICU for > 48 h undergoing therapy for one or more acute organ system failure or requiring intensive post-operative monitoring was studied. Detailed clinical history and investigations of each patient was recorded prospectively and analyzed.

2.4. Collection of samples

Relevant clinical samples depending on organ system involvement were collected as: urine, sputum, tracheal aspirate, urinary catheter, endotracheal tube, abdominal drains. All samples were inoculated on Sabouraud dextrose agar slants containing gentamicin (0.02 mg/mL) and cycloheximide (0.5%). One set of inoculated slants was incubated at 25 °C and the other at 37 °C, and they were examined every other day for growth up to 4–6 weeks.

2.5. Microscopy, culture and identification

Identification and speciation of the isolates were done by colony morphology, Gram's staining, germ tube formation, corn meal agar with Tween 80, HiCrome *Candida* agar and enzymatic triphenyltetrazolium chloride reduction test. For further characterization each isolate was subjected to carbohydrate assimilation and fermentation tests as per standard recommended procedures [9].

2.6. Antifungal susceptibility test

The *in vitro* minimal inhibitory concentrations (MICs) of the fluconazole and amphotericin B was done by the broth microdilution method as per Clinical and Laboratory Standards Institute (CLSI) M27-A3 document using Roswell Park Memorial Institute medium and 3-(N-morpholino) propane sulfonic acid buffer. The concentration ranges tested were 0.125–128.000 μg/mL for fluconazole and 0.016–16.000 μg/mL for amphotericin B. *Candida parapsilosis* (ATCC 22019) (*C. parapsilosis*) and *Candida krusei* (ATCC 6258) (*C. krusei*) from the American Type Culture Collection (ATCC) used as quality control with each batch of clinical isolates [10]. The MIC breakpoints recommended by CLSI guidelines were followed [10]. For fluconazole, MIC breakpoints were as follows: sensitive (MIC 8 μg/mL); susceptible-dose dependent (MIC 16–32 μg/mL); resistant (MIC ≥ 64 μg/mL). For amphotericin B, isolates with MICs of 1 μg/mL were categorized as resistant [10].

3. Results

The age (mean ± SD) of the patients was 37.90 ± 17.20 years (range 8–81 years). *Candida* colonization was seen in 57.3% patients, with 90 *Candida* isolates from different samples (Figure 1).

The majority of patients (77%) had one or more risk factors at the time of the diagnosis of candidiasis (Table 1). The mean age of patients with candidiasis (case group) was higher than the patients admitted to the same ICU with no candidiasis (control group). Case group was divided into two sub-groups: first (CG1) – patients with *C. albicans* colonization and second (CG2) – patients with NAC colonization. The time of hospital stay (mean) in CG2 (19.5 days) > CG1 (9.8 days) > controls (6.3 days) with no statistically significant difference. In control, CG1 and CG2 group, the percentage of patients with an indwelling device and prolonged antibiotic therapy was significantly higher than control and CG1 group

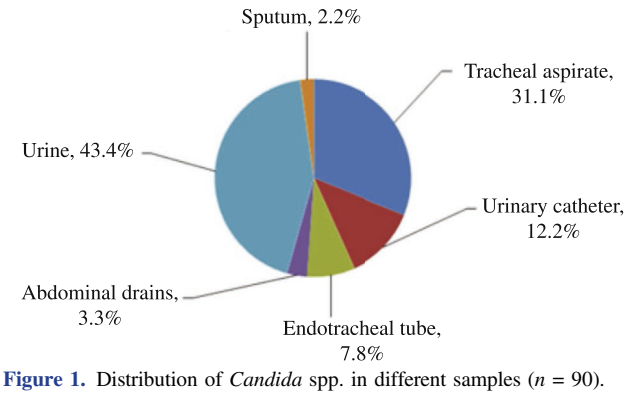

Figure 1. Distribution of *Candida* spp. in different samples (n = 90).