Abstract

Context: Candidiasis still remains as a common opportunistic infection in patients with human immunodeficiency virus (HIV). Drug resistance has become a serious health concern because of indiscriminate usage and dosage. Aim: To determine the antifungal resistance pattern of Candida albicans and non-albicans Candida (NAC) from HIV patients. Subjects and Methods: The study was carried out in the department of microbiology at a tertiary care hospital. Candida isolates obtained from HIV patients were tested for drug susceptibility by Vitek-2 automated system. Results: Antifungal susceptibility pattern (n=109) revealed that 15% of the isolates were resistant to at-least one and 85% were sensitive to all the drugs tested. About 10% and 19% of C. albicans showed resistance to fluconazole and flucytosine respectively. Among non-albicans tested, only C. tropicalis (14%) exhibited resistance to flucytosine. Conclusions: Knowledge on epidemiology, species prevalence, and drug resistance pattern may guide for effective therapy. This reduces morbidity and also improves the quality of life.

Key Words: Antifungal resistance, Candida albicans, HIV, non-albicans

Introduction

The low CD4+ T lymphocyte count in HIV patients invites the risk of acquired immunodeficiency syndrome (AIDS). Though the introduction of antiretroviral therapy has a major impact, candidiasis still remains a common opportunistic infection. Increased infections, prolonged use of antifungals to treat recurrent infections and the emergence of antifungal resistance have created the need for antifungal susceptibility testing.[1,2] The knowledge about the effects and burden of antifungal resistance is less compared to that of antibiotic-resistant bacterial infections, which are widely recognized as a public health problem.[3] This highlights the need to understand the reasons for their emergence, create awareness among medical and public health communities about these infections, and greater attention to prevent and control them.

Some species of Candida are becoming increasingly resistant to first-line and second-line antifungal medications, namely, fluconazole and echinocandins—anidulafungin, caspofungin, and micafungin.[3] Candida species vary in their susceptibility to different antifungals, so there is a need for an accurate and rapid identification for proper management and emergence of drug resistance.[1,5] The cause for the drug resistance could be several, such as immunological status of the patients, improper usage of drugs; also studies have shown antibacterial medications contributing to antifungal resistance, i.e., reduction of normal gut flora creating a favorable condition for opportunistic Candida.[4]

With this perspective, the present work was carried to understand the drug resistance pattern of Candida isolates obtained from our previous studies.[7]

Materials and Methods

The study was carried out in a tertiary care hospital, after obtaining ethical clearance. Informed consent was obtained from HIV seropositive subjects who were suspected to be co-infected with Candida.

Candida isolates obtained from HIV patients from our previous study[7] were the study material. Stored cultures were revived using Sabouraud dextrose medium. Individual colonies of each isolate were used for
susceptibility testing. Both albicans and non-albicans Candida isolates were processed for antifungal susceptibility test using Vitek-2 automated system using antimicrobial susceptibility testing (AST) card according to the manufacturer’s instructions. The result was obtained according to the breakpoints provided by the Vitek-2 system for amphotericin B (susceptible [S], \( \leq 1 \) \( \mu \)g/mL; intermediate, 2 \( \mu \)g/mL; resistant [R], \( \geq 4 \) \( \mu \)g/mL), fluconazole (S, \( \leq 8 \) \( \mu \)g/mL; susceptible dose-dependence [SDD], 16 to 32 \( \mu \)g/mL; R, \( \geq 64 \) \( \mu \)g/mL), caspofungin (S \( \leq 0.25 \) \( \mu \)g/mL; R, \( \geq 4 \) \( \mu \)g/mL), voriconazole (S, \( \leq 1 \) \( \mu \)g/mL; SDD, 2 \( \mu \)g/mL; R, \( \geq 4 \) \( \mu \)g/mL) and flucytosine (S, \( \leq 4 \) \( \mu \)g/mL, intermediate, 8-16 \( \mu \)g/mL; R, \( \geq 32 \) \( \mu \)g/mL).

**Results**

Of the total 109 isolates processed, 42 were C. albicans and 67 were non-albicans Candida. Among NAC, 29 were C. tropicalis, 13 C. guilliermondii, 10 C. parapsilosis, 6 C. lusitaniae, 5 C. krusei, 2 C. dubliniensis and 2 C. glabrata. Out of the 109 isolates, 16 (15%) were resistant to at least one drug and 93 (85%) were sensitive to all the drugs tested. About 11% of C. albicans and 4% of NAC showed resistance. Among NAC, only C. tropicalis exhibited resistance. C. albicans showed resistance to both fluconazole and flucytosine; about 10% of C. albicans were resistant to fluconazole and 19% were resistant to flucytosine. Among the non-albicans, 14% of C. tropicalis were resistant to flucytosine. No isolates showed resistance to amphotericin B, voriconazole, and caspofungin.

**Discussion**

Candidiasis, being the most common fungal opportunistic infection in HIV patients, acts as an indicator of the onset of immunodeficiency. Diagnosis of candidiasis accompanying speciation and susceptibility with a proper therapeutic dosage can prevent the emergence of drug-resistant pathogen, disease progression, and complications. This is duly because, along with Candida albicans, NAC has already emerged as drug-resistant pathogens.

In this study, NAC predominated over C. albicans and C. tropicalis was the most isolated species among NAC. But only 11% of C. albicans exhibited resistance to fluconazole, which correlates with the studies by Castero et al. (8.5%) and Enwuru et al. (9.5%) but differed from the study by Magaldi et al. who reported 31.5% of the isolates resistant.[8-10]

Antifungal susceptibility studies reported 31.1% and 22.2% resistance to fluconazole among the NAC while our finding was only 4%.[11,12]

Several studies have reported fluconazole resistance in Candida species from HIV patients,[13-15] Satana et al. in 2010 reported that all isolates were sensitive to voriconazole, 65 (97%) to amphotericin B, 66 (98.5%) to fluconazole which was similar to our study but differed from other studies.[16-20]

Jung et al. reported 1.4% of Candida isolates were resistant to fluconazole, 0.9% to voriconazole, and 97.3% to flucytosine resistant.[14] Pfaller et al. had reported in 2003 that all fluconazole-resistant isolates (4%) were sensitive to caspofungin; the same team in 2006 reported that there was no significant change in caspofungin activity over the past 4 years and there was no difference in its activity geographically.[11,21] Caspofungin has excellent *in vitro* activity against invasive clinical isolates of Candida from centers worldwide. The present study found no evidence of the emergence of caspofungin resistance among isolates of Candida.

Some of the studies have shown low resistance or no resistance for amphotericin B, which is in accordance with our findings.[10,20,22,23]

The reported frequencies of C. dubliniensis resistant to fluconazole were 19% and 18.2%; in the present study, both the isolates were sensitive.[24-25] Latiff et al. reported that 5% of the NAC isolates were resistant to flucytosine whereas our study found that 14% of C. tropicalis were resistant to flucytosine.[9]

**Conclusions**

The magnitude of the problem due to candidiasis in developing countries may be solved by knowing the epidemiology, species prevalence, and drug resistance pattern. This guides to provide effective therapy, reduces morbidity and also improves the quality of life.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

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