

Antifungal Resistance of *Candida Spp.* in Bloodstream Infection

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ABSTRACT

Objective: To investigate the distribution of fungal species causing bloodstream infection, and their antifungal resistance.

Methods: The descriptive cross-sectional study was conducted at Cho Ray Hospital, Ho Chi Minh city, Vietnam in 2018. All blood culture samples of patients which were positive with yeast were analyzed. Blood samples were taken to BD Bactec bottles and monitored in Bactec 9120 (Becton Dickinson, USA). Sub-cultures were performed on Sabouraud agar after the bottles flagged positive. The growth obtained after overnight incubation. Identification and drug susceptibility testing were performed by YST card and AST YS07 card on Vitek 2 Compact system (BioMerieux, France) according to CLSI standard.

Results: There were 89 patients who showed fungal positive blood culture results. Three leading pathogens caused bloodstream infection were *C. tropicalis* (31; 34.8%), *C. albicans* (20; 22.5%), *C. glabrata* (18; 20.2%). Resistance of *Candida spp.* to Fluconazole was highest (8; 9.9%), followed by Amphotericin B (7; 8.6%), Voriconazole (7; 8.6%), Flucytocine (1; 1.2%). Caspofungin and Micafungin showed no resistance.

Conclusion: The most common fungi in bloodstream infection were *C. tropicalis*, *C. albicans* and *C. glabrata*, respectively. The resistance to antifungus of *Candida spp.* strains was less than 10%. In this study, the resistance of *Candida spp.* to antifungal drugs was relatively low, however, it is necessary to continuously monitor the trend of drug resistance of fungal strains in order to detect changes in the resistant rates in order to handle appropriately.

Background

Candida spp. is a yeast that resides on the skin, in the gastrointestinal tract, urinary tract ... is the cause of opportunistic infection, causes disease in immunocompromised patients, patients treated with medical therapy and invasive surgery includes broad-spectrum antibiotics, chemicals and organ transplants [1,2]. *Candida spp.* can thrive in the intestine, break down the intestinal wall and enter the bloodstream. There are many toxins of *Candida* in bloodstream infection, which are very dangerous for health and difficult to treat. Fungal infections of the bloodstream include several conditions such as *Candida* blood infection, endocarditis, meningitis and other forms of deep organ damages. Nearly 96% of

fungal infections were caused by *Candida spp.* [3,4]. Mortality due to *Candida* has been reported up to 40-50% [5,6]. *Candida spp.* is the top four causes of sepsis in hospitals, accounting for 9% of the total number of pathogenic microorganisms [7]. In India, according to the study of Vibhor Tak and colleagues, 43% of fatality was caused by fungal infections [2], in the study of Ying-Lien Chena et al, this rate was 40 to 70% [8]. In Vietnam, studies on fungal infections are limited and have not been paid attention like bacterial infections, with little data on antifungal drug resistance. In this study, we investigated the causative agents of antifungal blood infections and the situation of antifungal drug resistance.

Research Methods

The descriptive cross-sectional study was conducted at Cho Ray Hospital, Ho Chi Minh city, Vietnam, from January 1, 2018 to December 31, 2018. All blood culture samples of patients which were positive with yeast were analyzed. Blood samples were taken in BD Bactec bottle and monitored in the Bactec 9120 machine (Becton Dickinson, USA). Sub-cultures were performed on Sabouraud agar after the bottles flagged positive. The growth obtained after overnight incubation. It was further identified by YST card and performed antifungal by AST YS07 card on Vitek 2 Compact system (BioMerieux, France). YST card can identify most Candida species, AST YS07 card detects susceptibility of 6 antifungal drugs: Amphotericin B, Caspofungin, Flucytosine, Fluconazole, Micafungin and Voriconazole according to CLSI standard.

Results

Distribution of Fungal Species in Bloodstream Infection

There were 89 patients who were positive for fungal blood culture. *Candida tropicalis* was the most common causative species (31; 34.8%), followed by *C. albicans* (20; 22.5%), *C. glabrata* (18; 20.2%), *C. parapsilosis* (8; 9.0%), *Cryptococcus neoformans* (4; 4.5%), *C. guilliermondii* (3; 3.4%), *C. rugosa* (1; 1.1%), *Kodamaea ohmeri* (1; 1.1%), *Trichosporon asahii* (1; 1.1%), *C. spherica* (1; 1.1%) and *Trichosporon mucoides* (1; 1.1%) (Table 1).

Resistant Pattern of *Candida Spp.* in Bloodstream Infection

Resistant rate of *Candida spp.* was highest to Fluconazole (8; 9.9%), followed by Amphotericin B (7; 8.6%), Voriconazole (7; 8.6%), Flucytosine (1; 1.2%). Caspofungin and Micafungin showed no resistance (Figure 1).

Among 31 *C. tropicalis*, resistant isolates to Fluconazole and Voriconazole were 7 (22.6%) and 7 (22.6%).

Among 20 *C. albicans*, resistant isolates to Amphotericin B were 3 (15.0%). Among 18 *C. glabrata*, resistant isolates to Amphotericin B and Fluconazole were 2 (11.1%) and 1 (5.6%), respectively.

Discussion

There were 89 patients who showed positive blood cultures with fungi in 2018 at Cho Ray Hospital. The three leading species of fungal infection are *C. tropicalis* (34.8%), *C. albicans* (22.5%) and *C. glabrata* (20.2%), respectively (Table 1) while our data in 2017, the three leading agents of fungal infections were *C. tropicalis* (33%), *C. albicans* (27%) *C. parapsilosis* (14%), and the fourth were *C. glabrata* (12%). In recent years, *C. tropicalis* is the species with the highest proportion of *Candida* bloodstream infection in Cho Ray hospital. In other countries, *C. tropicalis* also accounted for the highest proportion of blood fungal infections, as in Taiwan, accounting for 41.9% [9], in India 39% [2], however in other parts of the country in India, *C. albicans* accounted for the highest rate of 48.57% [10] while *C. parapsilosis* took the highest rate (28.4%) in Italy [11]. The above results show that the distribution of fungal pathogens of bloodstream infection is different in vary geographical regions, even changes over the years. Resistant rate of *Candida spp.* in bloodstream infection was highest to Fluconazole (8; 9.9%), followed by Amphotericin B (7; 8.6%), Voriconazole (7; 8.6%), Flucytosine (1; 1.2%) [12]. Caspofungin and Micafungin showed no resistance (Figure 1).

Table 1: Distribution of fungal species in bloodstream infection.

Pathogens	Number	Percent
<i>Candida tropicalis</i>	31	34.80%
<i>Candida albicans</i>	20	22.50%
<i>Candida glabrata</i>	18	20.20%
<i>Candida parapsilosis</i>	8	9.00%
<i>Cryptococcus neoformans</i>	4	4.50%
<i>Candida guilliermondii</i>	3	3.40%
<i>Candida rugosa</i>	1	1.10%
<i>Kodamaea ohmeri</i>	1	1.10%
<i>Trichosporon asahii</i>	1	1.10%
<i>C. spherica</i>	1	1.10%
<i>Trichosporon mucoides</i>	1	1.10%
Total	89	100.00%

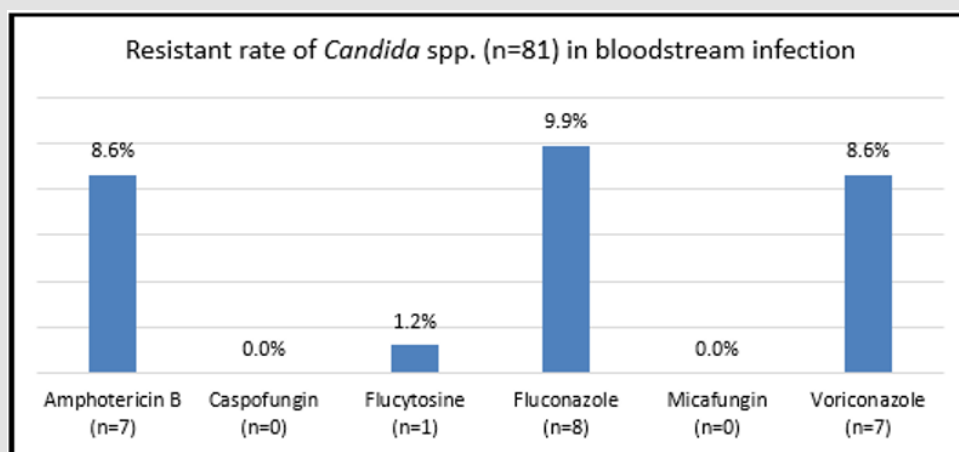


Figure 1: Resistance of *Candida spp.* in bloodstream infection.

The resistant rate of *C. tropicalis* to antifungal drugs in bloodstream infections was relatively high, resistance to Fluconazole was 22.6%, Voriconazole was also 22.6%, these rates are double higher than the rates in a study of Xu H, Yu SY, Zhou ML, et al. at Hospital in Central China: among *C. tropicalis* isolates, resistance rates to fluconazole and voriconazole were 11.9% and 7.7%, respectively (2012-2014) [1]. In the similar study in Taiwan, the resistance rate of *C. tropicalis* to Fluconazole was 13.9% (2011-2014) [9]. The high frequency of *C. tropicalis* and increasing trendazole non-susceptibility requires noting. The resistance rate of *C. albicans* to Amphotericin B is alarming (15.0%) because it is one of the main antifungal drugs for invasive candidemia and according to a study in China, *C. albicans* showed a wild type phenotype to Amphotericin B [1]. The resistant rates to *C. glabrata* of Amphotericin B and Fluconazole were 2 (11.1%) and 1 (5.6%), Voriconazole showed no resistant while in China resistant rates of Fluconazole and Voriconazole were 7.7% and 28.2%, perhaps the usage of Voriconazole is limited in our hospital, the susceptibility is still high [13].

Conclusion

The common pathogens causing fungal infections in Cho Ray Hospital in 2018 are *C. tropicalis*, *C. albicans*, *C. glabrata* and *C. parapsilosis*. The resistance of *Candida spp.* was highest to Fluconazole, followed by Voriconazole and Amphotericin B. It is necessary to implement good hospital fungal infection control and strict antifungal management policies to help reduce fungal infections, resistance and death of patients due to fungal infections. This study provided local data of pathogen distribution and antifungal susceptibilities of invasive yeast species, which is essential for guiding antifungal treatment [14].

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