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ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA

Distribution of Candida species isolated from blood cultures in a university hospital

Bir üniversite hastanesinde kan kültürlerinden izole edilen Candida türlerinin dağılımı

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ABSTRACT

Objective: Candidemia is the fourth most common infection among nosocomial blood circulation infections. Although *Candida albicans* is the most frequently identified species in invasive candidiasis, incidence of non-albicans Candida species were increased especially among critically ill patients. This reflects the changes in clinical practice. The main objective of the present study is to determine the distribution of the Candida species that causes candidemia in our hospital and contributes to the prevention of nosocomial infections.

Methods: In a retrospective study (2013-2014) on candidemia, various Candida species isolated from blood cultures were evaluated and their epidemiological, clinical, and microbiological characteristics were determined.

Results: A total of 200 species of Candida were identified and the distribution was as follows: 38% *C. albicans*, 24.5% *C. parapsilosis*, 16.5% *C. tropicalis*, 13% *C. glabrata*, 3% *C. krusei*, 2% *C. sake*, 1% *C. lusitaniae*, 0.5% *C. guilliermondii*. The highest amounts of (103/200; 51.5%) of Candida species were identified at the adult intensive care unit.

Conclusion: Parallel to the increase in the patient population that is as risk for Candida infections, epidemiological studies should be made to identify the species and develop effective treatment protocols.

Key words: Candida, candidemia, invasive candida infection, epidemiology

ÖZET

Amaç: Kandidemi, nozokomiyal kan dolaşımı enfeksiyonları arasında dördüncü sırada yer almaktadır. İnvaziv kandidiyazda *Candida albicans* halen en sık tanımlanan patojen olsa da, albicans dışı kandida türlerine bağlı enfeksiyonlarda dramatik artış dikkati çekmektedir bu durum, klinik uygulamadaki değişimleri yansıtmaktadır. Bu çalışmanın temel amacı kandidemi etkeni Candida türlerinin hastanemizdeki dağılımını belirleyerek hastane enfeksiyonlarının önlenmesine katkıda bulunmaktır.

Yöntemler: Retrospektif (2013-2014) bu çalışmada kan kültürlerinden izole edilen Candida türlerinin epidemiyolojik, klinik ve mikrobiyolojik karakteristikleri bildirilmiştir.

Bulgular: Toplam 200 Candida spp türü %38 *C. albicans*, %24,5 *C. parapsilosis*, %16,5 *C. tropicalis*, %13 *C. glabrata*, %3 *C. krusei*, %2 *C. sake*, %1 *C. lusitaniae*, %0,5 *C. guilliermondii* olarak tanımlanmıştır. Tanımlanan Candida türleri en yüksek oranla (103/200; %51,5) yoğun bakım ünitesinde saptanmıştır.

Sonuç: Candida infeksiyonları için risk teşkil eden hasta popülasyonunun artmasına paralel olarak, türlerin tanımlanması ve etkin tedavi protokollerinin geliştirilmesi için epidemiyolojik çalışmaların yapılması gerekmektedir.

Anahtar kelimeler: Candida, kandidemi, invaziv kandida infeksiyonu, epidemiyoloji

INTRODUCTION

The Candida species are opportunistic pathogenic organisms that exist in the normal flora of human skin and mucosa, but they may also develop superficial and severe systemic infections in the presence of predisposing factors. According to the findings of the Centers for Disease Control and Prevention (CDC), fungal infections are held responsible for 13% of all nosocomial infections [1].Eighty-two point three percent of Candida species are isolated in all fungemia cases. Among these species, *Candida albicans* (*C. albicans*) is the most common, with an identification rate of 64%.

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The clinical presentation of the presence of Candida species in blood is referred to as candidemia. The rate of candidemia in 76 countries was reported to be 6.9/1000 in the EPIC II study performed in 2011 [2]. In the United States, Candida species are the fourth most commonly isolated microorganism causing nosocomial blood circulation infections (BCI) and the third most commonly isolated microorganism causing the BCIs in intensive care units [3].

Reasons underlying the development of candidemia include the common use of wide spectrum antibiotics and immunosuppressive agents in the immunosuppressed patients and patients hospitalized in the intensive care units, long-lasting neutropenia due to cytotoxic therapy, and the use of central venous catheters [4]. In order to reduce mortality, clinicians use antifungal prophylaxis or preemptive treatment in patient groups with high risk. The use of azole analogues in these patients results in a reduction in the rate of species having low minimum inhibitory concentration (MIC) values, such as *C. albicans*, but an increase in the rate of species that are less susceptible to these antifungals, such as *C. krusei* and *C. glabrata*. Therefore, the epidemiology of the candidemia varies based on the antifungals used. Knowing the epidemiology of candidemia infections provides useful information about their prevalence and the routes of transmission.

In the present study, the Candida species isolated from the blood culture samples were evaluated.

METHODS

This retrospective study was obtained from a university hospital with 1300 beds. Patients with a high risk of candidemia, including patients receiving hemopoietic transplantation, patients who have neutropenia, patients who use wide spectrum antibiotics or immunosuppressive treatment and who have undergone surgical operation January 2013- December 2014 were included in the study.

Two bottles were used in the culturing for every patient. The 5-10 mL of blood was obtained from each patient under sterile conditions and inoculated in BACTEC automatic blood culture system (Becton Dickinson, USA), medium bottles. After a positive signal was obtained from the BACTEC automatic blood culture system inoculation was performed from the bottles in which yeast cells had been detected by gram staining, to Sabouraud Dextrose Agar (SDA, Oxoid, England) culture media with or without antibiotics. Colonies that were reproduced on the SDA after 24 hours of incubation in an aerobic medium were passed to CHROMagar Candida medium (HiMedia Laboratories, Mumbai, India) to identify the isolates. In addition, yeasts were respectively inoculated to Corn Meal Tween-80 Agar (Oxoid Ltd., Basingstoke, UK) and human serum to examine the structures of hyphae and blastoconidia, in addition to the development of germ tubes. All of the isolates having green colonies on CHROMagar Candida medium, developing chlamydospores on Corn Meal Tween-80 Agar, being germ tube positive, and the ability to reproduce at 45°C were considered to be *C. albicans* [5].

The identification of the yeasts other than *C. albicans* on the species level was done based on microscopic and macroscopic morphologies, urea hydrolysis, reproduction temperature, cycloheximide susceptibility and carbohydrate used the API ID 32C yeast identification system (Biomerieux, Marcy l'Etoile, France). The study protocol was approved by the Local Ethics Committee.

RESULTS

A total of 200 species of Candida were identified and the distribution was as follows: 38% *C. albicans*, 24.5% *C. parapsilosis*, 16.5% *C. tropicalis*, 13% *C. glabrata*, 3% *C. krusei*, 2% *C. sake*, 1% *C. lusitaniae*, 0.5% *C. guilliermondii*. The rate of non-albicans Candida was 62%. Although *C. albicans* was the most common species, the high rate of non-albicans Candida species is also remarkable.

The rates of isolation of the Candida species were most frequently (n=103; 51.5%) determined among the patients hospitalized at the intensive care unit, followed by the oncology department (n=24; 12%) and the infectious diseases department (n=13; 6.5%). *C. albicans* was the most commonly identified species in the intensive care unit (n=36; 35%). The distribution of Candida species which isolated in the same services was shown in Figure 1.

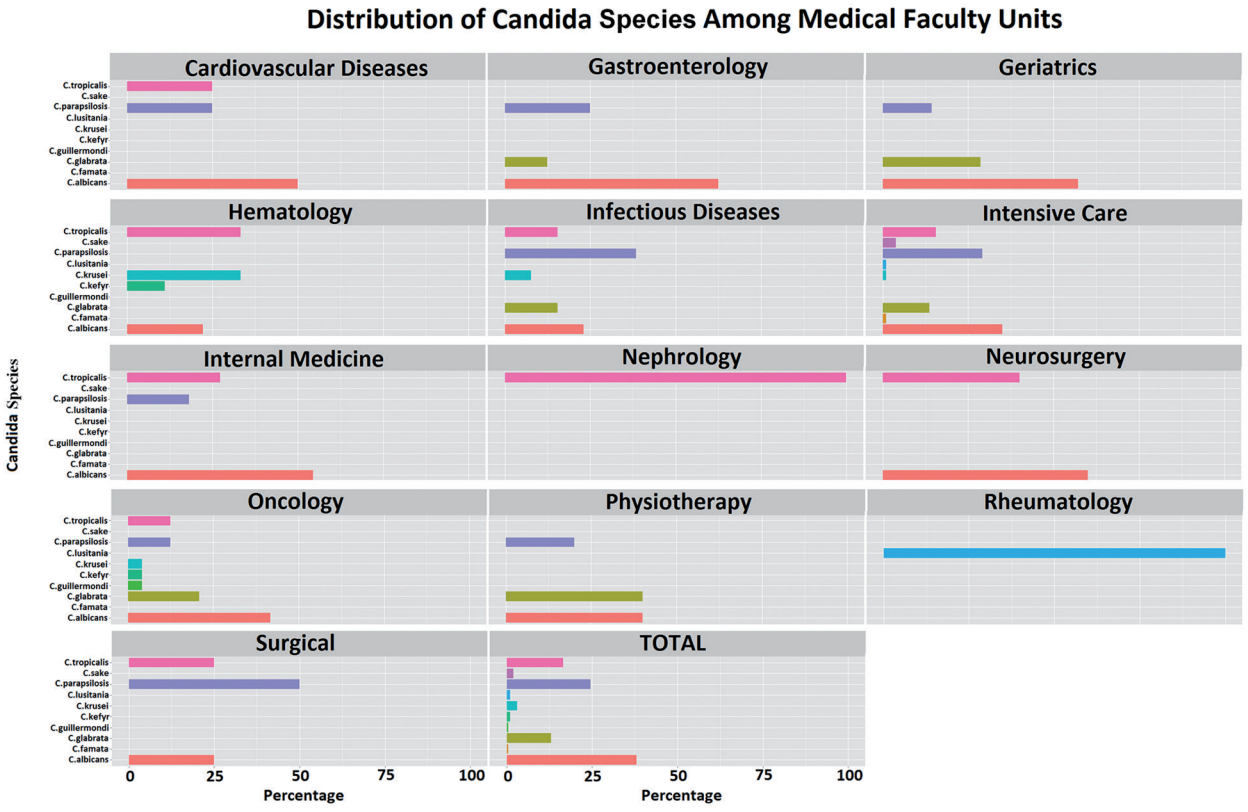

Figure 1. Distribution of Candida species in units of the Medical Faculty

DISCUSSION

Candidemia is a life threatening systemic fungal infection with a mortality rate of 38% [6]. Decreasing mortality depends on early onset of appropriate antifungal treatment. Fluconazole resistance of *C. krusei*, varying levels of fluconazole resistance of C. glabrata, and high MIC values seen in the echinocandins with *C. parapsilosis* species show that Candida should be identified at a species level in order to select the appropriate antifungal. Various national and international studies have been performed to define the epidemiology of candidemia.

In one of these international studies, Chen et al. [7] investigated candidemia episodes in 410 patients, and discovered that the most common pathogen was C albicans, followed respectively by *C. tropicalis, C. parapsilosis*, and *C. glabrata*. *C. tropicalis* was the most frequently identified species in another study that investigated the epidemiology of nosocomial candidemia infections, and mortality was reported to be highest among patients hospitalized in the oncology service [8].

Bouza et al. [9] reported that candidemia infections are caused by abdominal surgeries, acute renal failure, use of wide spectrum antibiotics, long periods of hospitalization in the intensive care unit, the use of corticosteroids and mucosal colonizations, and that prophylactic or empiric antifungal treatment may be initiated in the case of multifocal Candida colonization, or when the patient is under high risk of invasive candidiasis In another study investigating the effects of the *C. glabrata* species with high antifungal resistance in the intensive care units in Taiwan, the mortality rate of *C. glabrata* candidemia was reported to be 58% and fluconazole resistance of these species was found to be 11% [10].

In the GISIA-3 trial performed in 15 locations in Europe, *C. albicans* was reported to be the most frequent species, followed by *C. parapsilosis* and *C. glabrata* species, and mortality was shown to be higher among the infections caused by Candida species other than albicans [11]. In addition, it was underlined in this multi-center trial that *C. glabrata* species were more frequent in German speaking

countries, France, and Northern Europe, whereas *C. parapsilosis* species were more frequently observed in Turkey, Greece, and Spain. When data reported from Turkey is reviewed, the fact that *C. parapsilosis* species are the second most common species observed supports the GISIA-3 trial. When all BCIs were investigated in a study performed in Germany, it was seen that the Candida species is the fourth most common cause, as is the case in the United States, and the rate did not increase over the years [12]. In the same study, the *C. albicans*-related mortality rate was reported to be 21.9% and the non-albicans Candida-related mortality rate was reported to be 29.7% .

In a multi-center study performed in Poland, candidemia infections were most frequently seen in intensive care units and neonatal services, while *C. krusei* and *C. tropicalis* species were seen at a higher rate in the hematology services [13]. In a retrospective study performed by Bergamasco et al. [14] *C. parapsilosis* was reported to be the most common species identified in the patients with hematological malignancies, whereas *C. albicans* and *C. glabrata* were the most commonly isolated species among the patients with solid tumors.

In one of the similar studies performed in Turkey, Caliskan et al. [15] identified 58 Candida species using an automated identification system as follows: 57% C. albicans, 14% *C. parapsilosis*, 14% C. tropicalis, 10% C. glabrata, and 5% *C. guilliermondii*. Out of the identified species, 78% were reported in the patients under treatment in intensive care units and mostly in older patients. Atalay et al. (16) identified 97 Candida species from blood culture samples and reported that *C. albicans* was the most commonly isolated species, followed by *C. parapsilosis*. In addition, compared to their previous data, they have found that the increase in the Candida species in their hospital was in the favor of *C. parapsilosis*. Gultekin et al. [17] performed a study lasting seven years, and in line with the other studies, they found *C. albicans* to be the most common species; whereas there was also a dramatic increase in non-albicans Candida species observed within the last one year. In addition, contradictory to the other studies, candidemia cases were more frequently observed in internal diseases services of their hospital. Aslan et al. [18] reported that out of 136 Candida species in total, 51.5% were *C. albicans* and 48.5% were non-albicans Candida. They reported that the Candida species they isolated in their study was mostly (65.4%) from the services of the pediatric department. Kocak et al. [19] also reported that the most frequently isolated species were *C. albicans* (55.2%) and *C. parapsilosis* (28.9%), and the most common source of primary infection was the central venous catheter (39%). In the one-year study planned by Yapar et al. [20] 83 Candida species were isolated and the most frequently isolated species was *C. albicans*. The authors underlined that many invasive interventions played roles in the development of candidemia infections and these invasive interventions should be reduced.

When epidemiological data from different regions were compared to those obtained in our hospital, non-albicans Candida species were more frequent than the other species and the *C. parapsilosis* species was the second most frequent species among all. Based on distribution of the identified Candida species between the services at our hospital, the service in which these species were most frequently isolated was the intensive care unit, where invasive interventions were more frequently performed.

In conclusion, the causes of candidemia can vary from country to country, between years in the same country, and even between hospitals. For this reason, surveillance studies should be performed at regular intervals in all hospitals in order to manage the candidemia infections more effectively. Such studies can increase awareness of candidemia and the associated risk factors, and provide information about the future efficacy of the antifungals used.

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