J Surg Med. 2021;5(4):362-366.
DOI: 10.28982/josam.910783

Journal of Surgery and Medicine
e-ISSN=2602-2079

Retrospective assessment of fungal pathogens isolated from various clinical samples in a tertiary care hospital in Turkey: A cross-sectional study

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Ethics Committee Approval
Ethics approval was obtained from the Non-Interventional Clinical Research Ethics Committee of Karabuk University (No: 2021/529).
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

Financial Disclosure
The authors declared that this study has received no financial support.

Published
2021 April 16

Abstract

Background/Aim: Fungal infections are an emerging health problem worldwide and can be caused by a broad variety of fungal pathogens. This study aimed to retrospectively determine and evaluate the fungal pathogens isolated from various clinical samples in our laboratory.

Methods: A total of 996 clinical samples obtained from 803 patients who visited Karabuk University Training and Research Hospital microbiology laboratory between January 2019-December 2020 were included in this study. The BD-Phoenix 100 automated microbiology system was used for the identification of strains.

Results: Among 803 patients, 52.4% were female and 47.5% were male. The median age of the patients was 76 (0-99) years. Urine (49%) and blood (27.6%) samples were evaluated the most. The most common fungal pathogen was *Candida albicans* (48.7%), followed by *Candida tropicalis* (16.5%), *Candida parapsilosis* (10.6%), *Candida glabrata* (9%), *Saccharomyces cerevisiae* (5.7%), and *Trichosporon* species (3.1%). While more than 90% of fungal strains were isolated from the inpatients, 9% were isolated from the outpatients ($p<0.05$). Among all, 69.4% of strains were isolated from the intensive care units, followed by internal medicine (5.5%), palliative care (5%), urology (3.6%), and orthopedics and traumatology clinics (2.1%).

Conclusion: Although *C. albicans* is still the most common fungal pathogen, the incidences of non-albicans candida and other fungi are increasing worldwide. Therefore, each country should figure out its local fungal profile and update its antifungal treatment protocols accordingly.

Keywords: *Candida albicans*, *Candida tropicalis*, *Saccharomyces cerevisiae*, *Trichosporon asahii*

How to cite: Çolak M, Aşgın N. Retrospective assessment of fungal pathogens isolated from various clinical samples in a tertiary care hospital in Turkey: A cross-sectional study. J Surg Med. 2021;5(4):362-366.

Introduction

Fungal infections are an emerging health problem worldwide and can be caused by a broad range of fungi. They generally occur in immunosuppressive patients, but healthy individuals can also be infected by inoculation during invasive procedures or inhalation of fungal spores [1].

More than 100,000 fungal species are found and approximately three hundred are pathogenic for humans. However, only about 10-15% of pathogenic fungi usually cause systemic mycosis [2]. The pathogenic fungi, such as Blastomyces, Coccidioides, Paracoccidioides, Histoplasma, etc., have a restricted geographic distribution and cause clinical lesions in healthy humans. The opportunistic fungi, such as *Cryptococcus neoformans*, *Candida albicans*, etc., have a ubiquitous distribution and do not provide long-term immunity; hence, relapses are noted. Especially candidiasis and candidemia responsible for many opportunistic fungal infections [3,4]. Due to immune system disorders, *Candida* species (spp.) can cause candidemia and deep tissue infection. The isolation of *Candida* spp. from the urogenital, respiratory, and digestive systems is difficult to interpret. This is due to the presence of *Candida* spp. in the normal flora of the mucosal surface [5,6].

The risk of fungal infection increases in immunocompromised patients, such as those receiving cancer treatments, solid organ transplantation, corticosteroid, or chemotherapy treatment, in case of invasive procedures (catheter, dialysis, aspiration), some viral infections, burns, traumas, and among HIV-infected patients. The most important risk factors for these groups are prolonged use of broad-spectrum antibiotics, and colonization of mucosal surfaces and catheters [6].

Fungal infections can affect various organ systems and cause various clinical syndromes such as meningitis, sinusitis, osteomyelitis, granuloma, and brain abscess [3]. Recently, the increased frequency of hospital-acquired infections caused by opportunistic fungal pathogens is one of the great concerns.

Successful fungal infection management depends on the choice of an effective antifungal drug. The success of fungal treatment is firstly based on the accurate identification of the fungal pathogen. The diagnosis and treatment of fungal infections are challenging. Direct microscopic examination, routine stains, culture, serological and molecular tests obtained from the sterile sites of the body or through demonstration of fungal tissue invasion by histopathological examination aid in the diagnosis of fungal infection [7].

This study aimed to retrospectively determine and evaluate the fungal pathogens isolated from various clinical samples in our laboratory between 2019-2020.

Materials and methods

A total of 996 clinical samples obtained from 803 patients positive for fungal pathogens in Karabuk University Training and Research Hospital between January 2019- December 2020 were included in this cross-sectional study. If the same species was grown in simultaneous samples of the same patient, only one was included.

Blood and sterile body fluids were inoculated in BD-BACTEC Plus vials (Becton-Dickinson, USA) and incubated in BACTEC FX fully automated blood culture system for seven days. Other samples were cultured on 5% sheep blood agar (BD), chocolate agar (BD), Eosin Methylene Blue agar (BD), and Sabouraud dextrose agar (BD), and then incubated at 37 °C for 24-48 hours. The strains determined as yeasts in Gram staining were identified with the BD- Phoenix^{TM} 100 (Becton Dickinson, USA) automated system.

Statistical analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS for IBM-PC 20.0; SPSS Inc., USA). Descriptive statistics were given as number (n), percentage (%), and median values. The Kolmogorov–Smirnov test was used to determine whether the variables were normally distributed. For the comparison of continuous variables, two-sample t-test was used. The Pearson's Chi-squared test or Fisher's Exact test was used for comparison of categorical variables if applicable. A probability (*P*) value of <0.05 was considered statistically significant at a 95% confidence interval.

Results

Among 803 patients, 52.4% (421/803) were female and 47.5% (382/803) were male. The median age of the patients was 76 (0-99) years. The distribution of the numbers and age ranges of patients are shown in Table 1.

Table 1: The number of gender and age of the patients

Age	Female	Male	Total	Mean (SD)
0-20	7	7	14	8.3 (7.1)
21-40	27	8	35	30 (5.8)
41-60	66	51	117	53.8 (5.2)
61-70	63	87	150	66.3 (2.6)
> 71	258	229	487	80.7 (6.2)
Total	421	382	803	70.6 (16.6)

SD: Standard deviation

The most common fungal pathogen was *Candida albicans* with 48.7% (485/996). *Candida tropicalis* was detected in 16.5% (164/996), *Candida parapsilosis*, in 10.6% (106/996), *Candida glabrata*, *in* 9% (90/996), and *Saccharomyces cerevisiae*, *in* 5.7% (57/996). *Candida lusitania*, *Trichosporon. asahii*, *Candida kefyr*, *Candida krusei* and *Trichosporon mucoides* were detected in 3.3%, 3%, 2.2%, 0.8%, 0.1%, retrospectively. The distribution of the isolated fungal pathogens is shown in Figure 1.

Figure 1: The distribution of the isolated fungal pathogens

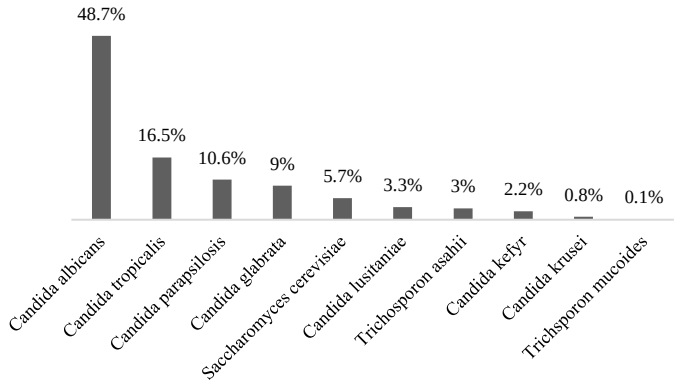

Table 2: The distribution of the samples according to the isolated fungal pathogens

Sample	Candida albicans n (%)	Candida. tropicalis n (%)	Candida parapsilosis n (%)	Candida glabrata n (%)	Saccharomyces cerevisiae n (%)	Candida lusitaniae n (%)	Trichosporon asahii n (%)	Candida kefyr n (%)	Candida krusei n (%)	Trichosporon mucoides n (%)	Total n (%)
Urine	235 (48.5)	75 (45.7)	18 (17)	43 (47.8)	50 (87.7)	20 (60.6)	30 (100)	14 (63.6)	3 (37.5)	-	488 (49)
Blood	111 (22.9)	63 (38.4)	63 (59.4)	28 (31.1)	1 (1.8)	7 (21.2)	-	1 (4.5)	1 (12.5)	-	276 (27.6)
ETA	77 (15.9)	7 (4.3)	8 (7.5)	10 (11.1)	5 (8.8)	4 (12.1)	-	5 (22.7)	2 (25)	-	118 (11.8)
Wound	9 (1.9)	10 (6.1)	2 (1.9)	7 (7.8)	-	-	-	1 (4.5)	-	-	29 (2.9)
Sputum	21 (4.3)	2 (1.2)	-	1 (1.1)	1 (1.8)	-	-	-	-	1 (100)	26 (2.6)
External Ear	5(1)	1 (0.6)	6 (5.7)	-	-	-	-	-	2(25)	-	18 (1.8)
Vagina	16 (3.3)	1 (0.6)	-	-	-	-	-	-	-	-	17 (1.7)
Catheter	3 (0.6)	4 (2.4)	3 (2.8)	1 (1.1)		1 (3)		-	-	-	12 (1.2)
BAL	8 (1.6)	-	1 (0.9)	-	-	1 (3)	-	1 (4.5)	-	-	11 (1.1)
Pleural Fluid	-	-	1 (0.9)	-	-	-	-	-	-	-	1 (0.1)
Total	485 (48.7)	164 (16.5)	106 (10.6)	90 (9)	57 (5.7)	33 (3.3)	30 (3)	22 (2.2)	8 (0.8)	1 (0.1)	996 (100)

Table 3: The distribution of isolated fungal pathogens according to clinics

Clinics	Candida albicans n (%)	Candida glabrata n (%)	Candida kefyr n (%)	Candida krusei n (%)	Candida lusitaniae n (%)	Candida parapsilosis n (%)	Candida tropicalis n (%)	Saccharomyces erevisiae n (%)	Trichosporon asahii n (%)	Trichsporon mucoides n (%)	Total n (%)
Intensive Care Units	328 (67.6)	50 (55.5)	16 (72.8)	4 (50)	30 (91)	76 (71.7)	128 (78)	39 (68.5)	19 (63.4)	1 (100)	691(69.4)
Internal Medicine	26 (5.3)	10 (11.2)	1 (4.5)	-	-	2 (1.9)	13 (8)	6 (10.5)	1 (3.3)	-	59 (5.9)
Palliative Care	28 (5.8)	1 (1.1)	-	-	2 (6)	9 (8.5)	7 (4.3)	5 (8.8)	2 (6.7)	-	54 (5.4)
Urology	18 (3.8)	6 (6.7)	1 (4.5)	1 (12.5)	-	3 (2.8)	2 (1.2)	1 (1.7)	5 (16.7)	-	36 (3.6)
Orthopedics and Traumatology	8 (1.6)	6 (6.7)	-	-	-	3 (2.8)	4 (2.5)	-	-	-	21 (2.1)
Chest Diseases	13 (2.7)	1 (1.1)	3 (13.7)	-	-	1 (0.9)	-	-	-		19 (1.9)
Otorhinolaryngology	6 (1.2)	-	-	2 (25)	-	10 (9.5)	1 (0.6)	-	-	-	19 (1.9)
Gynecology and Obstetrics	19 (3.9)	1 (1.1)	-	1 (12.5)	-	-	-	-	-	-	21 (2.1)
Nephrology	8 (1.6)	1 (11.1)	1 (4.5)	-	-	2 (1.9)	5 (3)	-	-	-	17 (1.7)
Oncology	4 (0.8)	6 (6.7)	-	-	-	-	-	-	-	-	10 (1)
Infectious Diseases	5 (1)	2 (2.2)	-	-	-	-	-	3 (5.3)	-	-	10 (1)
Pediatric Diseases	5 (1.1)	1 (1.1)	-	-	1 (3)	-	2 (1.2)	-	-	-	9 (0.9)
Emergency	6 (1.2)	1 (1.1)	-	-	-	-	-	-	-	-	7 (0.7)
Cardiology	3 (0.6)	1 (1.1)	-	-	-	-	1 (0.6)	2 (3.5)	2 (6.7)	-	9 (0.9)
Neurology	6 (1.2)	-	-	-	-	-	1 (0.6)	1 (1.7)	1 (3.3)	-	9 (0.9)
General surgery	1 (0.2)	2 (2.2)	-	-	-	-	-	-	-	-	3 (0.3)
Gastroenterology	1 (0.2)	-	-	-	-	-	-	-	-	-	1 (0.1)
Dermatology	0	1 (1.1)	-	-	-	-	-	-	-	-	1 (0.1)
Total	485	90	22	8	33	106	164	57	30	1	996(100)

The most common samples were urine (49%), and blood (27.6%), followed by endotracheal aspirate (ETA) (11.8%), and wound (2.9%). The other samples were sputum, external ear swab, vaginal swab, bronchoalveolar lavage fluid (BAL), and pleural fluid with 2.6%, 1.8%, 1.7%, 1.1%, and 0.1% respectively. Fungal pathogens were also isolated from catheters (1.2%). The distribution of the samples according to the isolated fungal pathogens is shown in Table 2. While 90.8% (n=729) of the strains were isolated from in-ward or intensive care patients, 9.2% (n=74) were isolated from outpatients. The distribution of the fungal pathogens was examined according to clinics, and there was a significant difference between outpatients and inpatients (P<0.05).

Fungal strain positivity was evaluated according to where the samples were received. Most positive samples were sent from the intensive care units (69.4%), followed by internal medicine, palliative care, urology, and orthopedics, and traumatology (5.5%, 5%, 3.6%, 2.1%, respectively). The distribution of isolated fungal pathogens according to the clinics is shown in Table 3.

Discussion

Fungal infections cause severe health concerns worldwide. Globally, more than a billion people are directly affected by mycoses, 150 million of which were exposed to life-threatening infections [8]. Candida spp. cause nosocomial infections, especially in critically ill patients admitted to the intensive care units. The mortality rate is between 15-35% depending on the *Candida* species [9]. Candida is a member of the skin flora, mucosa, and gastrointestinal system [9,10]. Mucosal colonization begins right away after birth, which is associated with an increased risk for endogenous infection. Candidemia is the most common systemic mycosis, and its incidence has gradually increased in the last two decades. Moreover, it has been reported as the fourth most common cause of nosocomial bloodstream infections [11]. This is associated with immune suppression, extensive use of invasive procedures, and intensive antibiotic treatment. In this study, *C. albicans* was the most isolated fungal pathogen from blood samples, with a rate of 40.2% (111/276). *C. tropicalis* and *C. parapsilosis* were each detected in 22.8% (63/276) and *C. glabrata* was detected in 10.2%. Similarly, *C. albicans* has been reported as the main fungal pathogen in blood samples in Turkey, with a rate ranging from 40% -57% [12-16]. Additionally, *C. tropicalis* and *C. parapsilosis* were reported as the 2nd and 3rd most common, respectively [13,16]. In 2571 blood samples isolated in France between 2002-2010, *C. albicans* constituted 56%, *C. glabrata*, 18.6%, *C. parapsilosis*, 11.5%, and *C. tropicalis*, 9.3% of bloodstream infections [17]. In a study conducted in China, the most common fungal pathogens isolated from blood cultures between 2007 and 2018 were *C. albicans, C. tropicalis, C. glabrata*, and *C. parapsilosis*, with rates of 43%, 18%, 12%, and 9%, respectively. It also was noted that the

prevalence of *C. albicans* decreased, while other *Candida* species were increased each year [18].

Falagas et al. have noticed that *C. albicans* is the predominant species worldwide, and its incidence was reported to range from 17% - 87% [19]. While the *C. albicans* incidence was highest in North and Central Europe and the US, non-albicans *Candida* spp. were more frequent in Asia, South America, and Southern Europe. Globally, the incidence of *C. albicans* decreased over time, while a rise in *C. tropicalis* and *C parapsilosis* infections were observed. *C. glabrata* and *C. krusei* infections remained stable [18,19]. The rising number of non-albicans *Candida* spp. such as *C. parapsilosis, C. glabrata, C. krusei, C. tropicalis* is worrisome. These species are primarily intrinsic and acquired resistance to azoles and echinocandins, agents used in the prophylaxis and treatment of *Candida* infections [11,19,20].

In this study, we isolated fungal pathogens mostly from urine samples. Fungal urinary infections have recently increased because of invasive surgical and medical procedures. Diabetes Mellitus, urinary tract anomalies, prolonged antibiotic use, and urinary catheterization are the main risk factors [21]. Renal candidiasis generally develops due to hematogenous spread in 80% of patients with candidiasis. Lower urinary infection often occurs due to dissemination from a catheter or the genital/gastrointestinal tract [21,22]. Most candiduria cases are asymptomatic. The presence of yeasts with leukocytes in the urine of symptomatic patients indicates an upper urinary tract infection [23] Although bacterial species are the main causes of urinary infections, fungal pathogens are the causative agents in 10%. Since *Candida* spp. can also be found in the genitourinary flora, it is challenging to decide whether there is contamination or colonization/infection in urine cultures. Cases of recurrent fungal growth should be evaluated with clinical findings [22-24].

In the present study, *C. albicans* was isolated from urine samples at a rate of 51% (235/488), followed by *C. tropicalis* (15.4%), *S. cerevisiae* (10.3%), *C. glabrata* (8.8%), *T. asahii* (6.2%) and *C. lusitania* (4.1%). Similarly, Karalti et al. isolated 54.2% *C. albicans* and 14.1% *C. tropicalis* from urine samples [24]. On the other hand, Atalay et al. mostly detected *C. albicans* and *C. glabrata* in urine samples at a rate of 30% [23]. It is noteworthy that *S. cerevisiae* is the third most common species in urine. We also isolated it from one blood sample and one ETA sample. Saccharomyces species is a ubiquitous colonizer of human mucosal surfaces. Saccharomyces spp. can colonize the urinary tract system in the setting of chronic disease, but these yeasts have rarely been determined to cause renal diseases such as a renal abscess or pyelonephritis [25]. Senneville et al. reported a case of *S. cerevisiae* fungus balls that were associated with total bilateral ureteral obstruction in a patient [26]. This yeast species is widely used in the food industry. However, it has been reported that it causes invasive infections in some patients who are given probiotics for diarrhea due to antibiotic use. Saccharomyces infections remain rare among invasive fungal infections, although the incidence has significantly increased since the 1990s [27]. Recently, Ventoulos et al. reported bloodstream infection by *Saccharomyces* in two patients hospitalized in the intensive care units, due to SARS CoV-2 infection, after *Saccharomyces* supplementation [28]. Also, *S. cerevisiae* can cause a wide range of human infections, such as pneumonia, liver abscess, esophagitis, peritonitis, cellulitis, urinary tract infection, and fungemia [29]. Therefore, *Saccharomyces* spp. must be considered an emerging fungal pathogen.

It is also remarkable that we isolated *Trichosporon* species at a rate of 6.2% in urine samples. *Trichosporon* spp. are basidiomycetous yeasts common in nature, also a part of the flora of the skin, respiratory and gastrointestinal tract [30]. They are causes of fatal infections in immunosuppressive patients, especially those with hematological cancers. *Trichosporon* infections have dramatically increased in recent years [31]. Urinary tract infections due to *T. asahii*, associated with indwelling medical devices, have been reported for years. Trichosporonosis has also been reported in immunocompetent patients with underlying peritoneal dialysis catheters, prosthetic valves, and urinary and intravenous catheters [32].

We isolated *C. albicans* in 67.9 % of respiratory samples. Non-*albicans Candida* species (*C. glabrata*, *C parapsilosis C. kefyr*, *C. tropicalis*, *C. krusei*, and *C. lusitaniae*) constituted 27.6% of other fungal strains, while other fungi (*S. cerevisiae* and *T. asahii)* made up 4.4%. Similarly, Sav et al. reported the most common fungal pathogen as *C. albicans* a rate of 76.8% among 849 fungal respiratory strains. The non-*albicans* frequency was 14.7% [33]. Candida spp. colonization is more common among critically ill patients. Candida airway colonization may facilitate bacterial colonization and subsequent development of bacterial pneumonia [34]. Respiratory Candida colonization in patients with ventilator-associated pneumonia was associated with longer mechanical ventilation duration and intensive care stay and higher 28-day mortality [35]. In other words, airway Candida colonization is a sign of poor prognosis.

Limitations

This is a retrospective single-center study based on laboratory data; therefore, the data of the clinical findings and treatments of patients are not available. In addition, antifungal susceptibility test results could not be included in the study, because the automated identification system does not have an antifungal test panel in our hospital. The prevalence of fungal pathogens belongs to a tertiary care hospital in the Western Black Sea region of Turkey, so the results may not reflect the general population of Turkey.

Conclusion

The profile of fungal pathogens that cause infections varies worldwide. In our study, although *C. albicans* was the predominant pathogen, the incidence of non-albicans Candida is worrying. Moreover, *Saccharomyces* spp. and *Trichosporon* spp. have emerged as causative agents in fungal infections. Therefore, the regional fungal pathogen profile should be determined and considered in the choice of empirical antifungal therapy.

References

1. Friedman DZ, Schwartz IS. Emerging fungal infections: new patients, new patterns, and new pathogens. J Fungi. 2019;5(3):67.
2. Sharma RR. Fungal infections of the nervous system: current perspective and controversies in management. Int J Surg. 2010;8(8):591-601.
3. Sanguinett M, Posteraro B, Beigelman-Aubry C, Lamoth F, Dunet V, Slavin M, et al. Diagnosis and treatment of invasive fungal infections: looking ahead. J Antimicrob Chemother. 2019;74(2):27-37.
4. Schwartz S, Kontoyiannis DP, Harrison T, Ruhnke M. Advances in the diagnosis and treatment of fungal infections of the CNS. Lancet Neurol. 2018;17(4):362-72.
5. Lagunes L, Rello J. Invasive candidiasis: from mycobiome to infection, therapy, and prevention. Eur J Clin Microbiol Infect Dis. 2016;35:1221–6.
6. Nami S, Aghebati-Maleki A, Morovati H, Aghebati-Maleki L. Current antifungal drugs and immunotherapeutic approaches as promising strategies to treatment of fungal diseases. Biomed Pharmacother. 2019;110:857-68.

7. Wiederhold NP, Patterson TF. What's new in antifungals: an update on the in-vitro activity and in-vivo efficacy of new and investigational antifungal agents. Curr Opin Infect Dis. 2015;28:539–45.
8. Ghosh PN, Fisher MC, Bates KA. Diagnosing Emerging Fungal Threats: A One Health Perspective. Front Genet. 2018;9:376.
9. Papon N, Courdavault V, Clastre M, Bennett RJ. Emerging and Emerged Pathogenic Candida Species: Beyond the Candida albicans Paradigm. PLoS Pathog. 2013;9(9):e1003550.
10. Kim J, Sudbery P. Candida albicans, a major human fungal pathogen. J Microbiol. 2011;49(2):171-7.
11. Pristov KE, Ghannoum MA. Resistance of Candida to azoles and echinocandins worldwide. Clin Microbiol Infect. 2019;25(7):792-8.
12. Coskun USS, Aksu N, Kursun S, Mumcuoglu I. Evaluation of Virulence Factors and Antifungal Susceptibility in Candida Strains İsolated From Blood Culture. Med J Gaziosmanpasa Univ. 2018;10(3):110-22.
13. Gultekin B, Eyigör M, Telli M, Aksoy M, Aydın N. A Retrospective Investigation of Candida Species Isolated from Blood Cultures during a Seven-year Period. ANKEM Derg. 2010;24(4):202-8.
14. Ozturk T, Ozseven A, Cetin E, Kaya S . Investigation of the Species and Antifungal Susceptibilities of Candida Strains Isolated from Blood Cultures. Kocatepe Med J. 2013;14(1):17-22.
15. Tumturk A. Risk factors, clinical characteristics, and mortality of candidemia in non-neutropenic, critically ill patients in a tertiary care hospital. J Surg Med. 2020;4(2):157-60.
16. Çaliskan E, Dede A, Biten Güven G. Distribution and Antifungal Susceptibilities of Candida Species Isolated from Blood Cultures. ANKEM Derg. 2013;27(1):25-30.
17. Lortholary O, Renaudat C, Sitbon K, Madec Y, Denoeud-Ndam L, Wolff M, et al. Worrisome trends in incidence and mortality of candidemia in intensive care units (Paris area, 2002-2010). Intensive Care Med. 2014;40(9):1303-12.
18. Xiao G, Liao W, Zhang Y, et al. Analysis of fungal bloodstream infection in intensive care units in the Meizhou region of China: species distribution and resistance and the risk factors for patient mortality. BMC Infect Dis. 2020;20:599.
19. Falagas ME, Roussos N, Vardakas KZ. Relative frequency of albicans and the various non-albicans Candida spp among candidemia isolates from inpatients in various parts of the world: a systematic review. Int J Infect Dis. 2010;14(11):e954-e966.
20. Bongomin F, Gago S, Oladele RO, Denning DW. Global and Multi-National Prevalence of Fungal Diseases-Estimate Precision. J Fungi. 2017;3(4):57.
21. Sobel JD, Fisher JF, Kauffman CA, Newman CA. Candida urinary tract infections--epidemiology. Clin Infect Dis. 2011;52:433-6.
22. Hollenbach E. To treat or not to treat--critically ill patients with candiduria. Mycoses. 2008;51(2):12-24.
23. Atalay MA, Koç AN, Sav H, Demir G. Candida species isolated from urine specimens and antifungal susceptibility in hospitalized patients Turk Hij Den Biyol Derg. 2013;70(4):185-90.
24. Karalti I. Retrospective Evaluation of Candida Species Isolated From Urine in a University Hospital. J Fungus. 2018;9(1):76-9.
25. Kiehn IE. Edwards FF, Armstrong D. The prevalence of yeasts in clinical specimens from cancer patients. Am J Clin PathoI. 1980;73:518.
26. Senneville E, Ajana F, Gerard Y, Bourez JM, Alfandari S, Chidiac C, Mouton Y, et al. Bilateral ureteral obstruction due to Saccharomyces cerevisiae fungus balls. Clin Infect Dis. 1996;23:636-7.
27. Enache-Angoulvant A, Hennequin C. Invasive Saccharomyces infection: a comprehensive review. Clin Infect Dis. 2005;41(11):1559-68.
28. Ventoulis I, Sarmourli T, Amoiridou P, Mantzana P, Exindari M, Gioula G, et al. Bloodstream Infection by Saccharomyces cerevisiae in Two COVID-19 Patients after Receiving Supplementation of Saccharomyces in the ICU. J Fungi (Basel). 2020;6(3):98.
29. Munoz P, Bouza E, Cuenca-Estrella M, Eiros JM, Pérez MJ, Sánchez-Somolinos M, et al. Saccharomyces cerevisiae fungemia: an emerging infectious disease. Clin Infect Dis. 2005;40(11):1625-34.
30. Colombo AL, Padovan AC, Chaves GM. Current knowledge of Trichosporon spp. and Trichosporonosis. Clin Microbiol Rev. 2011;24(4):682-700.
31. Li H, Guo M, Wang C, Li Y, Fernandez AM, Ferraro TN, et al. Epidemiological study of Trichosporon asahii infections over the past 23 years. Epidemiol Infect. 2020;148:e169.
32. Sun W, Su J, Xu S, Yan D. Trichosporon asahii causing nosocomial urinary tract infections in intensive care unit patients: genotypes, virulence factors and antifungal susceptibility testing. J Med Microbiol. 2012;61(12):1750-7.
33. Sav H, Demir G, Atalay MA, Koç AN. Evaluation of Candida strains isolated from clinical specimens. Turk Hij Den Biyol Derg, 2013;70(4):175-80.
34. Liu J, Yu YT, Xu CH, Chen DC. Candida Colonization in the Respiratory Tract: What Is the Significance? Front Med (Lausanne). 2021;7:598037.
35. Huang D, Qi M, Hu Y, Yu M, Liang Z. The impact of Candida spp airway colonization on clinical outcomes in patients with ventilator-associated pneumonia: A systematic review and meta-analysis. Am J Infect Control. 2020;48(6):695-701.

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