Original Article
J Immunol Clin Microbiol. 2020;5(1):35-40

J Immunol Clin Microbiol

Evaluation of Healthcare-Related Candida Infections That Develop in the Medical Intensive Care Unit

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Abstract

Background: The objective of this retrospective study was to evaluate healthcare-related Candida infections and factors related mortality.

Materials and Methods: Patients who were followed-up in the Medical intensive care unit (ICU) between 2015 and 2018 were retrospectively evaluated. Data were obtained by active surveillance method based on patient and laboratory. Statistical analysis of the data was performed using the SPSS 22 package program. The number, percentage, mean ± standard deviation and chi-square (χ^2) test were used to analyze the distribution of the data obtained. $p < 0.05$ was considered statistically significant.

Results: Fifty-nine (5.8%) of the 1018 patients who were followed up and treated in ICU developed Candida infection. The mean age was 73.9 ± 11.5. 39 patients (66.1%) with urinary catheter-related urinary tract infection, 12 (20.3%) patients with Laboratory Proven Blood Circulation Infection, 6 (10.2%) patients Abscess / soft tissue infection and 2 (3.4%) patients were diagnosed as Central Venous Catheter-Associated Blood Stream Infection. 36 (61%) of Candida species isolated from cultures were *C. albicans*, 8 (13.6%) were *C. parapsilosis*, 6 (10.2%) were *C. glabrata*, 6 (10.2%) were *C. tropicalis*, 1 (1.7%) in *C.crusei* and 2 (3.3%) were not identified species. 31 (52.5%) of the patients died. Total parenteral nutrition (p: 0.026) and mechanical ventilation (p: 0.004) were statistically significant. There was no statistically significant difference between candida species and mortality (p = 0.086).

Conclusions: Candida infections in ICUs are important causes of mortality. A good description of mortality related factors in Candida infections may lead to a decrease in mortality.

Key words: Intensive care unit, Candida infection, mortality related factors

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Introduction

Approximately 5-10% of hospitalized patients are followed and treated in the Intensive Care Unit (ICU). however, when all healthcare-related (SBI) infections are evaluated, it is seen that approximately 25% develop in ICUs. Length of hospital stay, severe diseases, presence of additional diseases (diabetes, chronic obstructive pulmonary disease, congestive heart failure), mechanical ventilation, invasive procedures such as urinary system catheter, central-peripheral venous catheter, insufficiency of ICU, surgical procedures, ICU The risk of infection increases due to poor cleaning, asepsis-antisepsis and insufficient compliance with hand hygiene rules (1, 2).

Many pathogens cause healthcare-related infections; Candida species follow bacteria such as *Staphylococcus aureus*, *Acinetobacter spp*., *Pseudomonas aeruginosa*. It is known that health-related candida infections are more common in patients hospitalized in the intensive care unit, increase morbidity and mortality, and increase the cost of treatment (1-17). However, there are few studies investigating factors related to mortality in healthcare related Candida infections. The objective of this retrospective study was to evaluate healthcare-related Candida infections that develop in the medical intensive care unit of a training hospital, Candida species distribution, mortality rate and mortality related factors.

Materials and Methods

This study was conducted retrospectively in 570-bed in a training hospital. Patients who were followed-up in the Internal Medicine ICU between January 01, 2015, and December 31, 2018, and diagnosed with Candida infection related to health care were included in the study. Data were obtained by active surveillance method based on patient and laboratory. Healthcare-related infection was diagnosed according to CDC diagnostic criteria (18).

Diagnostic Methods

Urine and blood samples were sent to Sabouraud Dectrosis Agar (SDA, Oxoid, UK) with antibiotics and without antibiotics, and incubated for 24 hours in both 25°C and 37°C ovens. The identification of breeding fungus Candida species was carried out by Germ tube, Chromagar conventional and Phoenix (Becton-Dickinson, USA) commercial method.

Statistical Analysis

Statistical analysis of the data was performed using the Statistical Package for Social Science (SPSS) 22 package program. The number, percentage, mean ± standard deviation and chi-square (χ^2) test were used to analyze the distribution of the data obtained. $p < 0.05$ was considered statistically significant.

Results

Fifty-nine (5.8%) of the 1018 patients who were followed up and treated in the intensive care unit developed SBI Candida infection. Twenty-seven (45.8%) of the patients with Candida growth were male. The mean age was 73.9 ± 11.5 (min-max: 38-93). The mean length of hospitalization in ICU was 23.5 ± 12.4 (min-max: 2-85) and the average hospitalization day in which infection developed was 14.4 ± 10.0 (min-max: 3-51). The mortality rate was 52.5% (n = 31) in patients with infection.

Clinic of patients, results of culture samples taken from patients and according to CDC diagnostic criteria, 39 patients (66.1%) with urinary catheter-related urinary tract infection, 12 (20.3%) patients with Laboratory Proven Blood Stream Infection (LP-BSI), 6 (10.2%)

patients Abscess / soft tissue infection and 2 (3.4%) patients were diagnosed as Central Venous Catheter-Associated Blood Stream Infection (CCV-BSII).

36 (61%) of Candida species isolated from cultures were *C. albicans*, 8 (13.6%) were *C. parapsilosis*, 6 (10.2%) were *C. glabrata*, 6 (10.2%) were *C. tropicalis*, 1 (1.7%) in *C. crusei* and 2 (3.3%) were not identified species (Table 1).

31 (52.5%) of the patients died. Mortality-related risk factors were shown in Table 2, and total parenteral nutrition (p: 0.026) and mechanical ventilation (p: 0.004) were statistically significant. When the mortality according to Candida species was examined, it was found that 18 of 36 patients with *C. albicans* growth died and 13 of 23 patients with non-albicans growth died. However, there was no statistically significant difference between Candida species and mortality (p = 0.086).

Table 1. Distribution of healthcare related Candida infections.

Location of the Infection	***C. albicans***	***C. glabrata***	***C. crusei***	***C. parapsilosis***	***C. tropicalis***	**Species not determined**	**Total**
Catheter-related urinary tract infection	25 (%64.1)	3 (%7.7)	1 (%2.6)	4 (%10.3)	4 (%10.3)	2 (%5.1)	39
Laboratory-proven bloodstream infection	6 (%50)	2 (%16.7)	0 (%0)	4 (%33.3)	0 (%0)	0 (%0)	12
Central venous catheter related blood stream infection	1 (%50)	0 (%0)	0 (%0)	0 (%0)	1 (%50)	0 (%0)	2
Abscess	4 (%)	1 (%16.7)	0 (%0)	0 (%0)	1 (%16.7)	0 (%0)	6

Table 2. Demographics of patients and factors related mortality.

Variable	***Total (n:59)***	***Survived (n:28)***	***Death(n:31)***	***P***
Age	73.9±11.5	73.7±12.9	74.1±10.4	0.899
Male	27	10 (%37)	17 (%63)	0.141
Concomitant diseases				
Diabetes mellitus	19	8 (%42.1)	11 (%57.9)	0.570
COPD	18	8 (%44.4)	10 (%55.6)	0.759
Cerebrovascular disease	22	10 (%45.5)	12 (%54.5)	0.812
Chronic renal failure	15	7 (%46.7)	8 (%53.3)	0.943
malignancy	16	5(%31.3)	11 (%68.8)	0.128
Acute renal failure	12	3 (%25)	9 (%75)	0.081
Extrinsic factors				
Urinary system catheter	57	28 (%49.1)	29 (%50.9)	0.171
Total parenteral nutrition	40	15 (%37.5)	25 (%62.5)	0.026
Central venous catheter	50	22 (%44)	28 (%56)	0.210

Blood transfusion	56	26 (%46.4)	30 (%53.6)	0.494
Mechanical ventilation	24	6 (%25)	18 (%75)	0.004
Surgery	7	5 (%71.4)	2 (%28.6)	0.176
Nutrition with Peg	25	10 (%40)	15 (%60)	0.325
Hemodialysis	14	4 (%28.6)	10 (%71.4)	0.105
Colostomy	7	3 (%42.9)	4 (%57.1)	0.795

Discussion

Fungal infections with high mortality and morbidity are gaining importance as they are increasingly detected in intensive care units (1). In our study, the mortality rate was 52.5% in patients who developed hospital-acquired candida infection in the internal medicine intensive care unit. In similar studies conducted in our country, it was found that the mortality of Candida isolated patients ranged between 14.6-83.3% (9, 12, 13, 19). In studies conducted abroad, it was found that mortality varies between 28.3-30.1% (10, 11, 17).

Many risk factors for candida infections have been described in the literature. Long-term hospitalization in the ICU, renal failure, diabetes, high APACHE score, antibiotic use, central venous catheter, total parenteral nutrition, surgical procedures, hematologic malignity, neutropenia, solid tumor, bone marrow transplantation, and candida colonization are some of these risk factors (3 -17). However, few studies are evaluating mortality-related factors in patients with Candida infection associated with health care. Mechanical ventilation and total parenteral nutrition is a defined risk factor for candida infections and it was found significant in terms of mortality in our study. Since our study is a retrospective, it was thought that there may be a relationship between general status of patients and these factors, although APACHE, etc. scoring which evaluates the general status of the patients is not performed. Canela and collegues (4) reported previous antibiotic therapy, followed by urinary catheterisation, central venous access, surgical procedures, parenteral nutrition and neutropenia as the risk factors associated with mortality. Accordingly, a study observed associations of 86.8% with antibiotic therapy, 86.3% with catheterisation and 34.3% with parenteral nutrition (6). Another study reported associations of 34.3% with surgical procedures, 69.1% with parenteral nutrition, 84.4% with intravascular devices and 91% with antibiotic therapy (7).

In our study, 36 (61%) of the isolated Candida spp. from the patients followed in the intensive care unit were *C. albicans*, 8 (13.6%) were *C. parapsilosis*, 6 (10.2%) were *C. glabrata*, 6 (10.2%) *C. tropicalis*, 1 (1.7%) *C. crusei*, while 2 (3.3%) species were not identified. . When the studies conducted in our country were examined, Kiraz and collegues (9) retrospectively evaluated the distribution of clinical *Candida spp*. isolated over a 5-year period in their hospital. Overall 3,756 *Candida spp*. were recovered from 10,857 specimens. *C. albicans* was isolated frequently from non-sterile body specimens while non-*C. albicans Candida spp*. were commonly recovered from sterile body specimens. Isolation rates of *C. albicans* were 83%, 61.2% and 49% in non-sterile body specimens, sterile body specimens and blood-sterile body fluids, respectively. Ece and collegues (5) evaluated the

distribution of 337 Candida isolates at in a training hospital between 2010 and 2013. They consisted of urine, blood culture, respiratory specimen and wound. The most isolated yeast strains were *C. albicans* (38.6%), *C. tropicalis* (13.9%), *C. parapsilosis* (28.4%), *C. glabrata* (7.4%), *C. krusei* (3.8%). When the international literature is examined; Sasso and collegues (6) evaluated the data retrospectively in a cohort study of 186 intensive care unit patients from 2007 to 2016 in a university hospital. They reported invasive Candida infections (n:244); 43% were intraabdominal and 22% bloodstream infections. *C. albicans* was the most frequent Candida species. This followed by *C. glabrata* (14.1%), *C. tropicalis* (10%) *C. parapsilosis* (8%) and *C. crusei* (5.3%). Lindberg and colleagues (14) evaluated Candida species from blood cultures collected from patients with septisemia between 2013 and 2016. Candida species were 0.1% of all the blood cultures collected from patients. Overall, 233 isolates were collected from 143 patients (84 males and 59 females). The fungal species distribution was as follows. *C. albicans*, 93 (65%); *C. glabrata*, 27 (19%); *C. parapsilosis*, 15 (10%); *C. dubliniensis*, 6 (4%); *C. tropicalis*, 4 (3%); *C. krusei*, 3 (2%); and others (*C. kefyr*, *C. lusitaniae*, *C. sake* and *C. pelliculosa*), 4 (3%).

Conclusion

The distribution of Candida species isolated from cultures in hospitals seems to vary according to regions and hospitals, and each hospital should follow its surveillance data. In conclusion, Candida infections associated with health care in intensive care units are important causes of morbidity and mortality (20, 21). A good description of mortality related factors in Candida infections may lead to a decrease in mortality in this patient group.

Ethics Committee Approval: NA
Informed Consent: NA
Peer-review: Externally peer-reviewed.
Conflict of Interest: No conflict of interest was declared by the author.
Financial Disclosure: The author declared that this study has received no financial support.

References

1. Trilla A. Epidemiology of nosocomial infections in adult intensive care units. Intensive Care Med. 1994; 20: 1-4.
2. Duel G, Fabry J, Nicolle L. Prevention of nosocomialinfection. In: Duel G, Fabry J, Nicolle L, eds. Prevention of hospital-acquired infections. A Practical Guide 2nd ed. Malta: World Health Organization, 2002: 30-8.
3. Dasgupta S, Das S, Chawan NS, Hazra A. Nasocomial infections in the intensive care unit: incidance, risk factors, outcome and associated pathogens in a public tertiary teaching hospital of Eastern India. Indian J Crit Care Med, 2015; 19(1): 14-20.
4. Canela HMS, Cardoso B, Vitali LH, Coelho HC, Martinez R, Ferreira MEDS. Prevalence, virulence factors and antifungal susceptibility of Candida spp. İsolated from bloodstream infections in a tertiary care hospital in Brazil. Mycoses. 2018;61(1):11-21.
5. Ece G, Samlioglu P, Akkoclu G, Atalay S, Kose S. The evaluation of the distribution of yeasts like fungi 'candida species' at a tertiary care center in Western Turkey. Int J Med Sci. 2012;9(7):617-20.
6. Caggiano G, Coretti C, Bartolomeo N, Lovero G, De Giglio O, Montagna MT. Candida bloodstream infections in Italy: changing epidemiology during 16 years of surveillance. Biomed Res Int. 2015;2015:256580.

7. Bassetti M, Merelli M, Ansaldi F, de Florentiis D, Sartor A, Scarparo C, Callegari A, Righi E. Clinical and therapeutic aspects of candidemia: a five year single centre study. PLoS ONE. 2015;10:e0127534.
8. Erbay H, Yalcın AN, Serin S, Turgut H, Tomatir E, Cetin B, et al. Nosocomial infections in intensive care unit in a Turkish University Hospital: a 2-years survey. Intensive Care Med, 2003; 29: 1482-8.
9. Kiraz N, Oz Y. Species distribution and in vitro antifungal susceptibility of clinical Candida isolates from university hospital in Turkey over a 5-year period. Med Mycol. 2011;49(2):126-31.
10. Papadimitriou-Olivgeris M, Spiliopoulou A, Fligou F, Spiliopoulou I, Tanaseskou L, Karpetas G, et al. Risk factors and predictors of mortality of candidaemia among critically ill patients: role of antifungal prophylaxis in its development and in selection of non-albicans species. Infection, 2017;45(5):651-7.
11. Yang SP, Chen YY, Hsu HS, Wang FD, Chen LY, Fung CP. A risk factors analysis of healtcare-associated fungal infections in an intensive care unit: A retrospective cohort study. BMC InfectDis, 2013; 13: 10.
12. Etiz P, Kibar F, Ekenoglu Y, Yaman A. Kan kültürlerinden izole edilen Candida türlerinin dağılımı nın ve antifungal duyarlılıklarının retrospektif olarak değerlendirilmesi. ANKEM Derg. 2015;29(3):105-113.
13. Yenigün Koçak B, Kulağlu F, Çelik AD, Akata F. Bir üçüncü basamak hastanesinde erişkin kandidemi olgularının epidemiyolojik özellikleri ve risk faktörlerinin değerlendirilmesi. Mikrobiyol Bul. 2011; 45(3): 489-503.
14. Lindberg E, Hammarström H, Ataollahy N, Kondori N. Species distribution and antifungal susceptibilities of yeasts isolated from the blood samples pf patients with candidemia. Sci Rep. 2019;9(1):3838.
15. Sudan R. Report on the Burden of Endemic Health Care-Associated Infection Worldwide; A Systematic Review of the Literature. World Health Organization, 2011; 1-34. Available from: https://apps.who.int/iris/bitstream/handle/10665/80135/9789241501507_eng.pdf?sequence=1&isAllowed=y (accessed: 17.01.2020).
16. Sasso M, Roger C, Sasso M, Poujol H, Barbar S, Lefranrt JY, et al. Changes in the distribution of colonising and infecting Candida spp. isolates, antifungal drug consumption and susceptibility in a French intensive care unit: A 10-years study. Mycoses, 2017; 00: 1-11.
17. Klevens RM, Edwards JR, Richards CL, Horon TL, Gaynes RP, Pollock DA, et al. Estimating health care- associated infections and deaths in U.S. Hospital, 2002. Public Health Rep, 2007; 122(2): 160-6.
18. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of healthcare-associated infection and criteria for specific types of infections in the acute care setting. Am J Infect Control, 2008; 36: 309-32.
19. Adıgüzel N, Karakurt Z, Güngör G, Yazıcıoğlu Ö, Acartürk E, Soğukpınar Ö, et al. Mortality rates and risk factors associated with nosocomial candida infection in a respiratory intensive care unit. Tüberküloz Toraks Derg, 2010; 58(1): 35-43.
20. Wisplinghoff H, Ebbers J, Geurtz L, Stefanik D, Major Y, Edmond M, et al. Nosocomial bloodstream infections due to Candida spp. İn the USA: species distribution, clinical features and antifungal susceptibilities. Int J Antimicrob Agents 2014; 43: 78-81.
21. Arendrup MC, Sulim S, Holm A, Nielsen L, Nielsen SD, Knudsen JD, et al. Diagnostic issues, clinical characteristics, and outcomes for patients with fungemia. J Clin Microbiol 2011; 49: 3300-8.

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