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Evaluation of the prognostic factors for candidemia in a medical intensive care unit

Medikal yoğun bakım ünitesinde kandidemi ile ilişkili prognostik faktörlerin değerlendirilmesi

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Abstract

Aim: Infections with *Candida species* are an important cause of morbidity and mortality in intensive care units (ICUs). The studies about the prognostic factors related with candidemia in ICU patients are limited and lacking in our country. The aim of this study is to evaluate the epidemiology and prognostic factors for candidemia in adult patients admitted to a medical ICU.

Methods: This is a retrospective cohort study. A total of 693 patients who were followed for more than 48 hours in our 16-bedded medical ICU between 2016 October-2019 March were evaluated retrospectively and 60 candidemia patients were included in the study. The patients were divided into two groups according to ICU mortality (survivor vs. non-survivor) and compared to determine possible prognostic factors among Candida infection risk factors.

Results: The total incidence of candidemia was 46 per 1000 admissions. The most common fungal isolate was *Candida albicans* (57.5%). The 30-day mortality was 71.7% and ICU-mortality was 78.3%. There was no difference for age, gender, co-morbid diseases, SOFA and APACHE II scores, Glasgow Coma Score, immunosuppressive treatments (steroid or chemotherapy), septic shock, neutropenia, acute hepatic or renal failure, need for vasopressors, hemodialysis, erythrocyte transfusion and total parenteral nutrition between groups. No relationship was found between the time of initiation of antifungal therapy and mortality (P=0.268). Survivors had shorter ICU stay and hospital stay before ICU, and lower Charlson Comorbidity Index scores than non-survivors (P=0.039, P=0.008, P=0.02, respectively). Length of hospital stay before ICU, need for invasive mechanical ventilation and hypoalbuminemia were the prognostic factors for ICU mortality of candidemia patients (P=0.034, P=0.013, P=0.029, respectively).

Conclusion: We reported the highest incidence rate of candidemia and one of the highest mortality rates in critically ill patients with candidemia. Confirming to most of the previous reports, *Candida albicans* (57.5%) was the most common isolate in our study. We evaluated reported risk factors for invasive candidiasis as a prognostic indicator for candidemia in ICU patients, and found that the length of hospital stay, invasive mechanical ventilation and hypoalbuminemia were prognostic indicators.

Keywords: Candidemia, Mortality, Critical care, Prognostic factors

Öz

Amaç: *Candida türleri* ile enfeksiyonlar, yoğun bakım ünitelerinde (YBÜ) önemli bir morbidite ve mortalite nedenidir. YBÜ hastalarında kandidemi ile ilişkili prognostik faktörlerle ilgili çalışmalar sınırlı sayıdadır ve ayrıca ülkemizde YBÜ'lerde kandidemi ile ilgili yeterli klinik çalışma bulunmamaktadır. Bu çalışmanın amacı, medikal bir YBÜ'ye kabul edilen yetişkin hastalarda kandideminin epidemiyolojisi ve prognostik faktörlerini değerlendirmektir.

Yöntemler: Bu çalışma retrospektif kohort bir çalışmadır. 2016 Ekim-2019 Mart tarihleri arasında 16 yataklı yoğun bakım ünitemizde 48 saatten fazla takip edilen 693 hasta retrospektif olarak değerlendirildi ve 60 kandidemili hasta çalışmaya dahil edildi. Hastalar YBÜ mortalitesine göre (sağ kalan ve ölen) iki gruba ayrıldı ve Candida enfeksiyon risk faktörleri arasından olası prognostik faktörleri belirlemek için karşılaştırıldı.

Bulgular: Toplam kandidemi insidansı 46 hasta/1000 başvuru olarak bulundu. En sık görülen mantar izolatı *Candida albicans*'tı (%57,5). Hastaların 30 günlük mortalitesi %71,7 ve YBÜ mortalitesi %78,3 olarak bulundu. Yaş, cinsiyet, eşlik eden hastalıklar, SOFA ve APACHE II skorları, Glasgow koma skoru, immünsüpresif tedaviler (steroid veya kemoterapi), septik şok, nötropeni, akut karaciğer veya böbrek yetmezliği, vazopresör ihtiyacı, hemodiyaliz, eritrosit transfüzyonu ve total parenteral beslenme bakımından gruplar arasında fark yoktu. Antifungal tedaviye başlama zamanı ile mortalite arasında ilişki bulunamadı (P=0.268). Sağ kalanlar YBÜ öncesinde daha kısa YBÜ yatış ve hastanede kalış süresine sahipti ve hayatta kalmayanlara göre Charlson Komorbidite İndeksi puanları daha düşüktü (sırasıyla P=0,039, P=0,008, P=0,02). Kandidemi hastalarının YBÜ mortalitesi için prognostik faktörler olarak YBÜ öncesi hastanede kalış süresi, invazif mekanik ventilasyon ihtiyacı ve hipoalbüminemi saptandı (sırasıyla P=0,034, P=0,013, P=0,029).

Sonuç: Kandidemili kritik hastalarda en yüksek kandidemi insidans oranını ve en yüksek ölüm oranlarından birini bildirdik. Daha önceki raporların çoğunu doğrular şekilde çalışmamızda en sık *Candida albicans* (%57,5) izolatı saptandı. YBÜ hastalarında kandidemi için prognostik bir gösterge olarak invaziv kandidiyaz için bildirilen risk faktörlerini değerlendirdik. Bunlardan hastanede kalış süresi, invazif mekanik ventilasyon ve hipoalbüminemi prognostik birer gösterge olarak bulundu.

Anahtar kelimeler: Kandidemi, Mortalite, Yoğun bakım, Prognostik faktörler

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Introduction

Candidemia is the fourth of the nosocomial bloodstream infection in intensive care units (ICUs). Although the rate of candidemia in ICUs varies between 3.5 and 34.3 per 1000 ICU admissions, it is gradually increasing [1-4]. In different studies in Turkey, candidemia is reported between 1.76 and 12.3 per 1000 individuals [3, 5]. Diagnosis and treatment are often delayed in patients with candidemia, leading to high mortality [6]. Reported candidemia mortality ranges from 30% to 72% [7-9]. While *Candida albicans* is the most frequently isolated *Candida species* in blood cultures, the frequency of non-albicans species has also been increasing in recent studies [10]. Identifying the risk factors of this infection with high mortality is important to prevent its development, detect patients at risk at its onset and start treatment early [1]. There are many studies on risk factors for candidemia in ICU patients, some of which report different results [3,5,11-14]. In these studies, long ICU stay, mechanical ventilation, total parenteral nutrition administration, broad spectrum antibiotic use, presence of diabetes mellitus, immunosuppression, steroid use, central venous catheter interventions, abdominal surgery, hemodialysis, sepsis or septic shock, high SOFA and APACHE II scores, and multiple site *Candida* isolations have been reported as possible risk factors for candidemia. However, the studies about the prognostic factors related with candidemia in ICU patients are limited [2,4,9,15-17].

As in all other ICUs, candidemia is an important cause of mortality in our ICU. In this study, we aimed to evaluate the epidemiology of candidemia cases and determine the effects of *Candida* risk factors on prognosis in patients with candidemia in our ICU.

Materials and methods

In this retrospective cohort study, we evaluated all patients followed between October 2016 and March 2019, in a 16-bedded ICU of a tertiary care hospital, Ondokuz Mayıs University, Faculty of Medicine. All patients ≥18 years-old, who were followed-up for more than 48 hours in the ICU and diagnosed with candidemia were included.

The age, gender, concomitant diseases, hospitalization before and after admission to the ICU, mortality, albumin levels, treatments (vasopressors, total parenteral nutrition, broad spectrum antimicrobial agents, antifungal treatments, erythrocyte transfusion, steroid use, chemotherapy in the last three months), and invasive procedures (invasive mechanical ventilation, central venous catheterization and hemodialysis) of the patients were noted from the hospital registry. Charlson Comorbidity Index, Glasgow Coma Score (GCS), disease severity scores by Acute Physiology and Chronic Health Evaluation II (APACHE II), and Sequential Organ Failure Assessment (SOFA) were also evaluated. Candidemia was defined as having signs and symptoms of infection and sepsis or septic shock, and at least one positive blood culture for Candida species. The patients were divided into two groups according to ICU mortality (survivor vs. non-survivor) and compared with regards to the effects of *Candida* infection risk factors on prognosis.

This study was performed in line with the principles of the Declaration of Helsinki and approved by the Ethics Committee of Ondokuz Mayıs University (2020/115).

Statistical analysis

Statistical Package for Social Sciences (SPSS), Version 25.0 was used for statistical analysis. The categorical parameters were given as frequency and percentages and compared by a Chi-square test. Parametric data were presented as mean (standard deviation) and independent samples t test was used for the comparison of two groups. Non-parametric data were given as median (interquartile range) and Mann-Whitney U test was used for the comparison of two groups. Logistic regression analysis (with backward elimination method) was used including variables, which were significant in bivariate analysis for mortality. The odds ratios (ORs) and their 95% confidence intervals (95% CIs) are presented. A *P*-value of <0.05 is considered significant.

Results

A total of 286 *Candida* isolates were recovered from 204 (29.4%) of 693 patients. Candidemia was present in 60 (8.7%). The total incidence rate of candidemia was 46 per 1000 admissions. The most common fungal isolate was *Candida albicans*, with 57.5% of the patients. The distribution of *Candida spp.* is shown in Table 1. *Candida* growth was first detected in the blood in 28 (46.7%) of the patients, in the urine in 22 (36.7%) patients, in the tracheal aspirate in 3 (5%) patients, in the central venous catheter in 12 (20%) patients, and in the body fluids in 2 (3.3%) patients.

Table 1: Comparison of isolated *Candida spp*

	All patients (n:60) n (%)	Survivors (n:13) n (%)	Non-Survivors (n:47) n (%)	*P*-value**
Candida albicans	42 (57.5)	10 (76.9)	32 (68.1)	0.538
Candida glabrata	8 (11.0)	2 (15.4)	6 (12.8)	0.806
Candida parapsilosis	7 (9.6)	1 (7.7)	6 (12.8)	0.614
Candida tropicalis	7 (9.6)	1 (7.7)	6 (12.8)	0.614
Candida keyfr	3 (4.1)	0	3 (6.4)	0.35
Candida krusei	2 (2.7)	0	2	0.449
Candida lusiteniae	2 (2.7)	0	2	0.449
Unknown spp*	2 (2.7)	0	2	0.449

* Two samples could not be specified. ** Pearson chi-square test for the comparison of categorized data was used.

The 30-day mortality rate was 71.7% (43 patients). When the mortality status of the patients was evaluated according to the status of discharge from the ICU, the mortality rate was 78.3% (47 patients). Evaluation of prognostic factors in patients was made according to ICU mortality. After positive cultures of *Candida*, 14 (29.8%) died in the first 7 days, 26 (55.3%) died within 7-30 days and 7 (14.9%) died after 30 days.

The comparison of survivor and non-survivor candidemia patients for demographic and medical factors and illness severity were shown in Tables 2 and 3. There were no differences in terms of age, gender, co-morbid diseases, SOFA, GCS and APACHE II scores, immunosuppressive treatments (steroid or chemotherapy), septic shock, neutropenia, acute hepatic or renal failure, need for vasopressors, hemodialysis, erythrocyte transfusion and total parenteral nutrition between groups. Survivors had shorter ICU and hospital stay before ICU, and lower Charlson Comorbidity Index scores than non-survivors (*P*=0.039, *P*=0.008, *P*=0.02, respectively). Colistin was the only antimicrobial agent which its previous use was

significantly associated with mortality in our study cohort (P=0.041).

Table 2: Age and the factors related with illness severity of the patients

Variables	All patients (n:60)	Survivors (n:13)	Non-Survivors (n:47)	*P*-value
Age (years)	65.3 (16)	62.2 (16.1)	66.2 (16.0)	0.423[a]
Length of ICU stay (days)	19 (23)	10 (18)	21 (22)	0.039[b]
Length of hospital stay before ICU (days)	13 (27)	3 (10)	17 (27)	0.008[b]
SOFA score	9.6 (3.1)	9.1 (4)	9.8 (2.8)	0.476[a]
APACHE II Score	24.8 (7.1)	21.9 (6.5)	25.6 (7.1)	0.098[a]
Glasgow Coma Score	9 (7)	12 (5)	8 (7)	0.06[b]
Charlson Comorbidity Index Score	3 (4)	2 (2)	3 (4)	0.02[b]
Time to start antifungal therapy after culture (days)	2 (1)	1 (1)	2 (1)	0.271[b]

ICU: Intensive care unit, SOFA: Sequential Organ Failure Assessment, APACHE II: Acute Physiology and Chronic Health Evaluation II. In parametric distribution, the data was given as mean (standard deviation) and independent samples t test [a] was used for the comparison of two groups. In non-parametric distribution, the data was given as median (interquartile range) and Mann-Whitney U test [b] was used for the comparison of two groups.

Table 3: Baseline characteristics and risk factors for mortality of patients with candidemia

Variables	All patients (n:60) n (%)	Survivors (n:13) n (%)	Non-Survivors (n:47) n (%)	*P*-value
Demographics				
Gender (Female)	32 (53.3)	9 (69.2)	23 (48.9)	0.194
Age≥ 65 years	33 (55)	7 (53.8)	26 (55.3)	0.925
Medical history				
Diabetes mellitus	14 (23.3)	2 (15.4)	12 (25.5)	0.444
Chronic pulmonary disease	4 (6.7)	0	4 (8.5)	0.276
Chronic renal disease	11 (18.3)	3 (23.1)	8 (17.0)	0.617
Chronic hepatic disease	2 (3.3)	0	2 (4.3)	0.611
Malignancy	33 (55)	7 (53.8)	26 (55.3)	0.925
Hematological	13 (21.7)	5 (38.5)	8 (17.0)	0.097
Solid tumor	20 (33.3)	2 (15.4)	18 (38.3)	0.121
Solid organ transplantation	3 (5)	1 (7.7)	2 (4.3)	0.615
Prior drug exposure				
Immunosuppressive therapy				
Steroid treatment	13 (21.7)	2 (15.4)	11 (23.4)	0.534
Chemotherapy	22 (36.7)	5 (38.5)	17 (36.2)	0.879
Broad-spectrum antimicrobial agents	60 (100)	13 (100)	47 (100)	-
Third generation cephalosporins	16 (26.7)	5 (38.5)	11 (23.4)	0.277
Beta lactam+beta lactamase inhibitors	36 (60.0)	6 (46.2)	30 (63.8)	0.250
Carbapenems	49 (81.7)	9 (69.2)	40 (85.1)	0.190
Glycopeptides	36 (60)	10 (76.9)	26 (55.3)	0.159
Quinolones	9 (15.0)	2 (15.4)	7 (14.9)	0.965
Aminoglycosides	10 (16.7)	1 (7.7)	9 (19.1)	0.436
Colistin	24 (40)	2 (15.4)	22 (46.8)	0.041
Antifungal treatment	55 (91.7)	13 (100)	42 (89.4)	0.219
Empirical	27 (45.0)	8 (61.5)	19 (40.4)	
After signal for culture positivity	28 (46.7)	5 (38.5)	23 (48.9)	0.268
None	5 (8.3)	0	5 (10.6)	
Antifungal agents				
Fluconazole	13 (21.7)	4 (30.8)	9 (19.1)	0.364
Echinocandin	42 (70.0)	9 (69.2)	33 (70.2)	
Other factors				
Septic shock	46 (76.7)	8 (61.5)	38 (80.9)	0.145
Neutropenia	11 (18.3)	4 (30.8)	7 (14.9)	0.190
Acute hepatic failure	5 (8.3)	1 (7.7)	4 (8.5)	0.925
Acute renal failure	33 (55)	8 (61.5)	25 (53.2)	0.592
Hemodialysis	29 (49.2)	5 (41.7)	24 (51.1)	0.561
Invasive mechanical ventilation	42 (70.0)	5 (38.5)	37 (78.7)	0.005
Need for vasopressors	46 (76.7)	8 (61.5)	38 (80.9)	0.145
Total parenteral nutrition	49 (81.7)	9 (69.2)	40 (85.1)	0.190
Hypoalbuminemia (albumin < 2.0 g/dL)	26 (43.3)	2 (15.4)	24 (51.1)	0.022
Central venous catheter	46 (76.7)	10 (76.9)	36 (76.6)	0.980
Erythrocyte transfusion	54 (90)	13 (100)	41 (87.2)	0.174
Multiple-site colonization with Candida spp	45 (75)	11 (84.6)	34 (72.3)	0.366
Tracheotomy	4 (6.7)	0	4 (8.5)	0.276

Examination of antifungal treatment revealed that five (8.3%) patients were not given any antifungal treatment, 27 (45%) patients were empirically treated after culture collection and 28 (46.7%) patients were administered antifungal treatment after yeast signal or growth in culture. No relationship was found between the time of initiation of antifungal therapy and mortality (P=0.268). Average antifungal treatment initiation time was 1.9 (1.4) days from the day of culture collection. It was observed that 13 (21.7%) of 55 patients who were given antifungal treatment were given fluconazole and 42 (70.0%) were given echinocandin.

All patients had previous use of broad-spectrum antimicrobial agents, a urinary catheter and gastric acid suppression before *Candida* growth, therefore, these factors could not be evaluated between the groups.

In Table 4, we evaluated the prognostic factors associated with ICU mortality for candidemia patients. In bivariate logistic regression analysis, backward elimination method was used and the variables included in the first step were length of hospital stay before ICU, length of ICU stay, APACHE II, SOFA and Charlson Comorbidity Index scores, previous use of Colistin, need for invasive mechanical ventilation and hypoalbuminemia. The results for variables retained in the final multivariable model are presented (Nagelkerke R^2=0.488). Length of hospital stay before ICU, need for invasive mechanical ventilation and hypoalbuminemia were the prognostic factors for ICU mortality of candidemia patients (P=0.034, P=0.013, P=0.029, respectively).

Table 4: Binary logistic regression analyses of prognostic factors associated with ICU mortality for candidemia patients.

Variables	Odds Ratio	95% CI	*P*-value
Length of hospital stay before ICU (days)	1.119	1.008-1.241	0.034
Need for invasive mechanical ventilation	7.887	1.541-40.358	0.013
Hypoalbuminemia (albumin <2.0 g/dL)	9.465	1.265-70.815	0.029

CI: Confidence Interval, ICU: Intensive care unit, SOFA: Sequential Organ Failure Assessment, APACHE II: Acute Physiology and Chronic Health Evaluation II.
Logistic Regression analysis backward elimination method was used and the variables included in the first step were length of hospital stay before ICU (days), length of ICU stay (days), APACHE II Score, SOFA Score, Charlson Comorbidity Index Score, previous use of Colistin, need for invasive mechanical ventilation and hypoalbuminemia (albumin <2.0 g/dL). Results for variables retained in the final multivariable model are presented (Nagelkerke R^2=0.488).

Discussion

In our study, the incidence of candidemia was 46 per 1000 admissions and this is the highest reported rate. The incidence rate of candidemia in ICUs varies between 3.5 and 34.3 per 1000 ICU admissions [1-4]. This high rate of candidemia may be due to backgrounds of our patients. The rate of malignancy was remarkably high, and all had previously used antimicrobial agents. We all know that alterations in host defense can result in an overgrowth of Candida, which is termed colonization. Antibiotic usage can provoke colonization by suppressing normal intestinal bacterial micro-flora, and allowing the proliferation of *Candida spp.*

The incidence of *Candida albicans* is around 50-60% in many studies [3,9,15,16,18]. Consistent with the literature, the most common *Candida species* in our patient cohort was *Candida albicans* (57.5%). However, there are studies in which *non-albicans Candida species* were reported more frequently. For example, *Candida tropicalis* in North India [19] and *Candida parapsilosis* in Thailand [20] and in China [2] were more common.

The 30-day mortality rate was 71.7% and ICU mortality rate was 78.3% in our study. This mortality rate is higher than most of the previous studies, in which it ranged from 30% to 72% [5,7-9,21]. Increased mortality was also reported in case of the need for mechanical ventilation [22]. We suggest that the possible reasons for the high mortality rate were the presence of severely ill patients with high APACHE II (24.8 (IQR:7.1)) and

SOFA (9.6 (IQR:3.1)) scores and very high malignancy rate (55%) in our study cohort. In addition, the hospitalization periods of our patients before ICU were long (13 days-interquartile range=27) and the rate of invasive mechanical ventilation (70%), which we found as a prognostic factor in mortality, was high in our patients.

In some studies, the mortality rate was higher in C*andida albicans* related candidemia than with non-*albicans Candida* spp [*4*]. In our study, the distribution of *Candida spp.* was not different between the groups. So, there was no difference between Candida spp. regarding mortality rate in our study, like some previous studies [9,16,23,24].

The risk factors associated with invasive candidiasis were well established [9,25] and the *Candida* score is a tool used widely for the diagnosis of invasive candidiasis [26]. We evaluated the effect of all previously reported risk factors on mortality. All patients had previous use of broad-spectrum antimicrobial agents, a urinary catheter and gastric acid suppression before *Candida* growth, therefore, these factors could not be evaluated between the groups. Candida score includes total parenteral nutrition, multifocal *Candida spp.* colonization and severe sepsis. In our study, no relationship was found between all these factors and mortality. Increased mortality in the presence of septic shock is an expected finding, and there are studies confirming this in patients with candidemia [17,27]. Although the rate of septic shock was higher in the non-survivor group (80.9% vs. 61.5%) in our study, this difference may not have reached the level of significance due to the small number of patients.

When chronic diseases were evaluated, Charlson Comorbidity Index, which is a chronic disease score, was significantly higher in non-survivors, although no effect of each chronic disease on mortality was detected. For the evaluation of the severity of illness we used SOFA and APACHE II scores and GCS. Although it was not significant, survivors had higher GCS and lower SOFA and APACHE II scores than non-survivors.

All our patients had a history of antimicrobial agent usage. Colistin was the only one that was significantly associated with mortality in our study cohort. This may be because of drug toxic effects and the resistant pathogens requiring Colistin use. There are different findings about the effect of steroid use on prognosis in patients with candidemia. There are studies reporting that it increases [2,13] or decreases mortality [17]. In our study, we could not detect any effect of the patient's prior steroid treatment or chemotherapy on mortality. In our study, there was no significant difference in the mortality rates of patients in terms of starting antifungal treatment earlier or receiving fluconazole or echinocandin treatments similar to previous studies [2,28].

The effect of hypoalbuminemia on mortality was evaluated in only one study [9] and no association was found in candidemia patients. However, we found that low albumin levels are associated with high mortality. We suggest that this may be related to both the fact that albumin is a negative acute phase reactant and the poor nutrition status of the patient.

As we mentioned before, the number of studies evaluating the factors affecting mortality in patients with candidemia is limited and the results are controversial. In an Italian multi-center study [17], risk factors associated with mortality were evaluated in internal medicine wards. They found the presence of septic shock and concomitant chronic kidney failure as risk factors associated with mortality in candidemia patients. Basetti et al. [27] evaluated the incidence and outcome of invasive candidiasis in ICUs in Europe and found that age, SOFA score, severe hepatic failure and septic shock were associated with increased mortality. Ala-Houhala et al. [28] reported that the severity of underlying illnesses, ICU stay at the onset of candidemia and older age (>65 years) were independent risk factors of mortality in candidemia. However, Gonzalez de Molina et al. [4] found that only APACHEII score was a predictor of mortality. In a study conducted with ICU patients in Japan [9], 25 patients with candidemia were divided into two groups as survivors and non-survivors, and the effect of candidemia risk factors on patient prognosis was evaluated. It was concluded that none of the 15 risk factors identified were associated with mortality, but the cumulative increase in the total number of risk factors was the most useful marker on prognosis.

In the comparison of groups according to mortality, length of ICU stay, hospital stay before ICU, Charlson Comorbidity Index score, concomitant Colistin use, need for invasive mechanical ventilation, and hypoalbuminemia were significantly associated with mortality. However, some of the variables did not retain significance at multivariable analysis. In logistic regression analysis, only three factors were associated with mortality, which included the length of hospital stay before ICU, need for invasive mechanical ventilation and hypoalbuminemia.

Limitations

The main limitations of our study included its retrospective and single-center nature, and lack of information regarding laboratory parameters such as beta-d-glucan. Patients were followed until discharge from the ICU. Despite this, we evaluated the effects of many risk factors on mortality in our study.

Conclusions

We reported the highest incidence rate and one of the highest mortality rates in critically ill patients with candidemia. The most common species was *Candida albicans*, concordant with most of the previous studies. We evaluated each risk factor reported for invasive candidiasis in terms of prognostic value for candidemia in ICU patients and found that only three (length of hospital stay, mechanical ventilation and hypoalbuminemia) could be considered prognostic indicators.

References

1. Bassetti M, Giacobbe DR, Vena A, Wolff M. Diagnosis and Treatment of Candidemia in the Intensive Care Unit. Semin Respir Crit Care Med. 2019;40(4):524–39.
2. Ding R, Ji Y, Liu B, Zhao D, Zhang X, Zhang Z, et al. Risk factors for mortality in cases of intensive care unit-acquired candidemia: a 5.5-year, single-center, retrospective study. Int J Clin Exp Med. 2018;11:9950–7.
3. Tukenmez Tigen E, Bilgin H, Perk Gurun H, Dogru A, Ozben B, Cerikcioglu N, et al. Risk factors, characteristics, and outcomes of candidemia in an adult intensive care unit in Turkey. Am J Infect Control. 2017;45(6):61–3.
4. Gonzalez de Molina FJ, Leon C, Ruiz-Santana S, Saavedra P, the CAVA I Study Group. Assessment of candidemia-attributable mortality in critically ill patients using propensity score matching analysis. Crit Care. 2012;16:R105.
5. Yapar N, Akan M, Avkan-Oguz V, Ergon CM, Hancer M, Doluca M. Risk factors, incidence and outcome of candidemia in a Turkish intensive care unit: a five-year retrospective cohort study. Anaesth Pain & Intensive Care. 2014;18(3):265–71.
6. Epelbaum O, Chasan R. Candidemia in the Intensive Care Unit. Clin Chest Med. 2017;38(3):493–509.
7. Wisplinghoff H, Bischoff T, Tallent SM, Seifert H, Wenzel RP, Edmond MB. Nosocomial bloodstream infections in US hospitals: analysis of 24,179 cases from a prospective nationwide surveillance study. Clin Infect Dis. 2004;39(3):309–17.

8. Andes DR, Safdar N, Baddley JW, Playford G, Reboli AC, Rex JH, et al. Impact of treatment strategy on outcomes in patients with candidemia and other forms of invasive candidiasis: a patient-level quantitative review of randomized trials. Clin Infect Dis. 2012;54(8):1110–22.
9. Kawano Y, Togawa A, Nakamura Y, Mizunuma M, Yamasaki R, Hoshino K, et al. Prognostic factors for candidaemia in intensive care unit patients: a retrospective analysis. Singapore Med J. 2017;58(4):196–200.
10. Guinea J. Global trends in the distribution of Candida species causing candidemia. Clin Microbiol Infect. 2014; 20 (6): 5–10.
11. Li F, Zhou M, Zou Z, Li W, Huang C, He Z. A risk prediction model for invasive fungal disease in critically ill patients in ICU. Asian Nurs Res. 2018;12(4):299. doi: 10.1016/j.anr.2018.11.004.
12. Arslan F, Caskurlu H, Sari S, Cankar Dal H, Turan S, Erturk B, et al. Risk factors for noncatheter-related Candida bloodstream infections in intensive care units: A multicenter case-control study. Med Mycol. 2019;57(6):668–74.
13. Falcone M, Tiseo G, Tascini C, Russo A, Sozio E, Raponi G, et al. Assessment of risk factors for candidemia in non-neutropenic patients hospitalized in Internal Medicine wards: A multicenter study. Eur J Intern Med. 2017;41:33–8.
14. da Silva RB, Neves RP , Hinrichsen SL, de Lima-Neto RG. Candidemia in a public hospital in Northeastern Brazil: Epidemiological features and risk factors in critically ill patients. Rev Iberoam Micol. 2019;36(4):181–5.
15. Leroy O, Gangneux JP, Montravers P, Mira JP, Gouin F, Sollet JP, et al. Epidemiology, management, and risk factors for death of invasive Candida infections in critical care: A multicenter, prospective, observational study in France (2005-2006). Crit Care Med. 2009;37:1612–8.
16. Ghrenassia E, Mokart DD, Mayaux J, Demoule A, Rezine I, Kerhuel L, et al. Candidemia in critically ill immunocompromised patients: Report of a retrospective multicenter cohort study. Ann Intensiv Care. 2019;9:62.
17. Sbrana F, Sozio E, Bassetti M, Ripoli A, Pieralli F, Azzini AM, et al. Independent risk factors for mortality in critically ill patients with candidemia on Italian Internal Medicine Wards. Intern Emerg Med. 2018;13(2):199–204. doi: 10.1007/s11739-017-1783-9.
18. Tümtürk 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.
19. Xess I, Jain N, Hasan F, Mandal P, Banarjee U. Epidemiology of candidemia in a tertiary care centre of north India: 5-year study. Infection. 2007;35:256–9.
20. Anunnatsiri S, Chetchotisakd P, Mootsikapun P. Fungemia in non-HIV infected patients: a five-year review. Int J Infect Dis. 2009;13:90–6.
21. Kollef M, Micek S, Hampton N, Doherty JA, Kumar A. Septic shock attributed to Candida infection: importance of empiric therapy and source control. Clin Infect Dis Off Publ Infect Dis Soc Am. 2012;54(12):1739–46.
22. Saillard C, Darmon M, Bisbal M, Sannini A, Chow-Chine L, Faucher M, et al. Critically ill allogenic HSCT patients in the intensive care unit: a systematic review and meta-analysis of prognostic factors of mortality. Bone Marrow Transpl. 2018;53:1233–41.
23. Bassetti M, Trecarichi EM, Righi E, Sanguinetti M, Bisio F, Posteraro B, et al. Incidence, risk factors, and predictors of outcome of candidemia. Survey in 2 Italian university hospitals. Diagn Microbiol Infect Dis. 2007;58:325–31.
24. Chow JK, Golan Y, Ruthazer R, Karchmer AW, Carmeli Y, Lichtenberg D, et al. Factors associated with candidemia caused by nonalbicans Candida species versus Candida albicans in the intensive care unit. Clin Infect Dis. 2008;46:1206–13.
25. Pfaller MA, Diekema DJ. Epidemiology of invasive candidiasis: a persistent public health problem. Clin Microbiol Rev. 2007;20:133–63.
26. León C, Ruiz-Santana S, Saavedra P, Almirante B, Nolla-Salas J, Alvarez-Lerma F, et al; EPCAN Study Group. A bedside scoring system ("Candida score") for early antifungal treatment in nonneutropenic critically ill patients with Candida colonization. Crit Care Med. 2006;34:730–7.
27. Bassetti M, Giacobbe DR, Vena A, Trucchi C, Ansaldi F, Antonelli M, et al. Incidence and outcome of invasive candidiasis in intensive care units (ICUs) in Europe: results of the EUCANDICU project. Critical Care. 2019;23:219. doi: 10.1186/s13054-019-2497–3.
28. Ala-Houhala M, Valkonen M, Kolho E, Friberg N, Anttila VJ. Clinical and microbiological factors associated with mortality in candidemia in adult patients 2007–2016. Infectious Diseases. 2019;51(11-12):824–30.

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