Mortality rates and risk factors associated with nosocomial *Candida* infection in a respiratory intensive care unit

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ÖZET

Solunumsal yoğun bakım ünitesinde Candida infeksiyonu risk faktörleri ve mortalite oranları

Bu çalışmanın amacı, solunumsal yoğun bakım ünitesi (YBÜ)'nde yatan hastalarda nozokomiyal Candida infeksiyon (NCİ) insidansı, risk faktörleri ve mortalite oranlarını saptamaktır. 2006 yılında solunumsal YBÜ'de yatarak tedavi gören 163 hastanın verileri geriye dönük olarak incelendi. NCİ; solunumsal YBÜ'de 1 günden uzun kalan, ciddi sepsisi olan hastalarda en az bir kez Candida spp. izole edilmesi olarak tanımlandı. NCİ olan ve olmayan hastalar invaziv işlemler, eşlik eden durumlar ve mortalite oranları açısından karşılaştırıldı. Risk faktörleri için lojistik regresyon analizi uygulandı. Hastaların 26 (%15.6)'sında NCİ saptandı ve ortalama yaşları 65 ± 15 olup kadın erkek oranı 8/18 idi. Candida albicans/Candida nonalbicans oranı 13/13 idi. Nozokomiyal mantar infeksiyonu olan hastalarda yoğun bakım kalış süresi daha uzun (48.2 ± 7.5 güne karşılık 10.3 ± 0.8 gün; p< 0.01) ve yoğun bakım mortalitesi daha yüksek saptandı (%14.6'ya karşılık %30.8; p< 0.05). NCİ için risk faktörleri; invaziv mekanik ventilasyon, santral ven kateter varlığı, total parenteral nütrisyon, çoklu antibiyotik kullanımı, ventilatörle ilişkili trakeobronşit (p< 0.001, odds ratio, %95 GA 6.27, 2.05-19.16; 28.3, 4.61-32.04; 10.93, 4.04-29.56; 2.12-88.98; 14.99, 5.6-40.08), sepsis ve ventilatörle ilişkili pnömoni (p< 0.01, 7.34, 1.66-32.35; 3.87, 1.42-10.52) bulundu. Nozokomiyal mantar infeksiyonu olgularımızda, invaziv mekanik ventilasyon, santral ven kateter varlığı ve infeksiyonu, total parenteral nütrisyon, çoklu antibiyotik kullanımı, ventilatörle ilişkili trakeobronşit, sepsis ve ventilatörle ilişkili pnömoni nozokomiyal mantar infeksiyonu için risk faktörlerini oluşturmaktadır. Nozokomiyal mantar infeksiyonu olan ve antifungal tedavi alan hastalarda uzun yoğun bakım kalış süresi ve yüksek mortalite oranı nedeniyle risk faktörleri dikkatlice saptanmalı ve tedbirler alınmalıdır.

Anahtar Kelimeler: *Yoğun bakımda yatan hasta, nozokomiyal kandidiyazis, invaziv prosedürler, risk faktörleri.*

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SUMMARY

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To determine the incidence and mortality rate of nosocomial Candida infections (NCI) with respect to associated risk factors in the respiratory intensive care unit (RICU) patients. Data of 163 RICU patients were analyzed for NCI in 2006 retrospectively. Diagnosis of NCI; at least one Candida spp. was isolated in patients with severe sepsis, hospitalized > 1 day intensive care unit (ICU). NCI positive vs. NCI negative were compared with respect to invasive procedure, comorbidities, mortality. Risk factors were analyzed by logistic regression test. NCI positive in 26 (15.9%) patients were mean age: 65 ± 15 years (female/male ratio: 8/18). Candida albicans/non-albicans ratio was 13/13. ICU stay was longer in NCI positive than NCI negative (48.2 ± 7.5 days vs. 10.3 ± 0.8 days; p< 0.001). Higher mortality rates were demonstrated in NCI positive (14.6% vs. 30.8%; p< 0.05). Risk factors for NCI were as follow: Invasive mechanical ventilations (IMV), central catheters and related infections, total parenteral nutrision, multiple antibiotics, ventilator associated tracheobronchitis (VAT) (p< 001 for all and, odd ratio: 95% CI: 6.27, 2.05-19.16; 28.3, 4.61-32.04; 10.93, 4.04-29.56; 2.12-88.98; 14.99, 5.6-40.08, respectively) and sepsis and ventilator associated pneumonia (VAP) (p< 0.01, 7.34, 1.66-32.35; 3.87, 1.42-10.52, respectively). Presence of chatheters and related infections, IMV, multiple antibiotics use, parenteral nutrision, VAT, sepsis and VAP were founded as major risk factors for our patients with NCI. Because of longer ICU duration and higher mortality in NCI patients with treated untifungal drugs, risk factors must be evaluated carefully in the ICU.

Key Words: *ICU patients, nosocomial candidiasis, invasive procedure, risk factors, Candida species, mortality.*

Among hospital-acquired pathogens, *Candida* species are encountered frequently in critically ill patients and become the fifth most frequent highly fatal nosocomial pathogen encountered in intensive care units (ICU), after pathogens such as *Enterobacteriaceae*, *Pseudomonas aeruginosa*, and *Staphylococcus* spp. (1-4). Invasive fungal infections (IFI) in ICU are of particular concern for many reasons, including the increasing prevalence of non-albicans species, the lack of suggestive specific sign and symptoms, the complexity of the patients' underlying conditions, the insidious presentation, and the high mortality, especially when prompt antifungal treatment is not administered (5-7). The criteria for IFI were defined by Ascioglu and co-workers for immunocompromised patients with cancer (8). This definition requires the presence of fungemia, specifically blood culture yielding fungi in patients with temporally related clinical signs and symptoms compatible with relevant organism. It also requires IFI to be present in other sites, to be confirmed histopathologically or cytopathologically, or fulfilling the following four criteria:

1. Positive culture result for samples obtained via sterile procedure from normally sterile sites, excluding urine and mucous membranes,

2. Compatible clinical and radiologic manifestations,

3. No evidence of infection caused by microorganisms other than fungus,

4. Improvement in signs and symptoms, and radiology after use of antifungal (8).

Differentiation between *Candida* colonization and invasive candidiasis is difficult. The "*Candida* score" has recently developed by Leon and co-workers (9). The *Candida* score calculated as follows (variables coded as absent 0, present 1): Total parenteral nutrition (TPN) x 1, plus surgery x 1, plus multifocal *Candida* colonization x 1, plus severe sepsis x 2 and *Candida* score ≥ 3 accurately selected patients at high risk for inva-

sive candidiasis (10). Very recently, a new study done by same authors for researching the usefulness of the "*Candida* score" for discriminating between *Candida* colonization and invasive candidiasis in non-neutropenic critically ill patients and, they founded that the patients with *Candida* score ≥ 3 had high risk for invasive candidiasis, was very accurate and treatment with antifungal drugs were crucial to prevent higher mortality (11).

In our study we used very similar criterias to define the *Candida* infections and prompt antifungal treatment and also to assess the risk factors and mortality rate associated with the nosocomial candidiasis and to determine the distribution of *Candida* spp. in a population of critically ill patients admitted to our respiratory ICU.

MATERIALS and METHODS

A retrospective cohort study was performed between January to December 2006 including 163 patients followed at respiratory ICU of the Sureyyapasa Chest Diseases and Chest Surgery Training and Research Hospital, Istanbul, Turkey which is a mid-size medical, with 10 beds.

Definitions

Nosocomial *Candida* infections: Diagnosis of nosocomial *Candida* infection (NCI) was based on as follows in our study:

1. Presence of at least one site culture positive for *Candida* spp. together with appropriate signs and symptoms of multifocal fungal infections (negative results for bacterial infections, fever unresponsive to medications, detoriated apperence, skin, nail, oromucosal-mouth, vaginitis with *Candida*).

2. Presence of severe sepsis criteria (sepsis was defined in accordance with the American College of Chest Physicians/Society of Critical Care Medicine consensus conference definition) (12).

3. Patient admitted for more than 24 hours in the ICU or seven days-hospital during a single hospitalization period.

Candidemia: Isolation of *Candida* spp. from blood culture (8).

Invasive *Candida* infection: *Candida* spp. were confirmed histopathologically or cytopathologically from samples (8).

Candidiasis was determined in terms of location (oropharynx, urine, or tracheal aspirates, blood), species (albicans vs. non-albicans), treatment and the entire duration of the stay in the ICU.

Colonisation was considered unifocal when *Candida* spp. were isolated from one body site colonized without any sign and symptoms of severe diseases, and multifocal when *Candida* spp. were simultaneously isolated from various foci.

Data Collections

Aiming to compare ICU patients with or without nosocomial *Candida* infections (NCI positive, NCI negative); detailed retrospective analysis of medical records was accomplished for all of the patients. Distribution of age, gender, underlying disease, past history of chronic systemic diseases (renal, cardiovascular, endocrine), and the frequency of invasive procedures (mechanical ventilator, catheterization, tracheostomi, TPN) were recorded. Infections secondary to invasive procedures such as ventilator associated tracheobronchitis (VAT), ventilator associated pneumonia (VAP), and sepsis was recorded considering their contribution to candidiasis development. The severity of illness on ICU admission was calculated by the Acute Physiology Assessment and Chronic Health Evaluation (APACHE) II score system (13).

Blood specimens were processed by automated blood culture systems (Bactec; Becton Dickinson, USA, and Bact/Alert; Organon Teknika, USA), and yeasts were identified with the use of the germ-tube reaction and the API 20C/API IDI 32C System (bioMérieux, France), supplemented with morphology confirmation on Sabouraud agar.

The present study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and approved by the institutional ethics committee.

Statistical Analysis

Data were analyzed using SPSS 13.0 programme. Analysis included the comparison of categorical and quantitative variables in patients with and without *Candida* infections, using the chi-square Fisher's tests for independent categorical variables and the Student's t-test or the Mann-Whitney U-test for the numerical variab-

Table 1. Comparison of ICU patients with or without NCI according to demographic features, present disorder and the underlying chronic systemic illness*.

		NCI negative [n= 137 (84%)]	NCI positive [n= 26 (15.9%)]	Total (n= 163)
Gender	Female	34 (20.9)	8 (4.9)	42 (25.8)
	Male	103 (63.2)	18 (11.0)	121 (74.2)
Age (year)		61.81 ± 1.20	65.58 ± 2.93	62.41 ± 1.1
	COPD	72 (44.2)	9 (5.5)	81 (49.7)
	Pneumonia	19 (11.7)	3 (1.8)	22 (13.5)
Present disorder	Malignancy	7 (4.3)	3 (1.8)	10 (6.1)
Diabetes mellitus	Absent	118 (72.4)	20 (12.3)	138 (84.7)
	Present	19 (11.7)	6 (3.7)	25 (15.3)
Renal disease	Absent	132 (81.0)	24 (14.7)	156 (95.7)
	Present	5 (3.1)	2 (1.2)	7 (4.3)
Cardiovascular disease	Absent	106 (65.0)	19 (11.7)	125 (76.7)
	Present	31 (19.0)	7 (4.3)	38 (23.3)

* Data are presented as n (%) or mean ± SD.
ICU: Intensive care unit, NCI: Nosocomial *Candida* infections, COPD: Chronic Obstructive Pulmonary disease.

Table 2. Comparison of patients with/out NCI according to invasive procedures, length of ICU stay and APACHE II score.

		NCI negative (n= 137)	NCI positive (n= 26)	Total (n= 163)
Catheter	Absent	112 (81.8)	7 (26.9)	119 (73.0)
	Present	25 (18.2)	19 (73.1)*	44 (27.0)
	Number	0.22 ± 0.04	1.54 ± 0.39[a]	0.43 ± 0.07
	Duration (day)	1.93 ± 0.52	24.54 ± 5.33*	5.58 ± 1.1
Mechanical ventilation	Absent	73 (53.3)	4 (15.4)	77 (47.2)
	Present	64 (46.7)	22 (84.6)*	86 (52.8)
	Duration (hour)	60.55 ± 11.3[a]	431.15 ± 135.2	119.6 ± 25.5
Tracheostomy	Absent	120 (87.6)	12 (46.2%)	132 (81.0)
	Present	17 (12.4)	14 (53.8%)*	31 (19.0)
Total parenteral nutrition	Absent	105 (76.6)	6 (23.1)	111 (68.1)
	Present	32 (23.4)	20 (76.9)*	52 (31.9)
	Duration (day)	1.84 ± 0.4[a]	9.50 ± 2.5	3.13 ± 0.5
Length of ICU stay (day)		10.27 ± 0.83	48.23 ± 7.52*	16.33 ± 1.75
APACHE II score	First	18.79 ± 0.6	21.23 ± 1.05	19.18 ± 0.54
	Last	10.03 ± 0.39	8.52 ± 1.25	9.8 ± 0.38
Leukocyte count		13145.16 ± 592.1	15476.0 ± 1867.5	13526 ± 523

* Data are presented as n (%) or mean ± SEM. [+]p< 0.05; [a]p< 0.01; and *p< 0.001. Chi-square test for independent categorical variables and Student's t-test for mean scores were used for the analysis.
NCI: Nosocomial *Candida* infections, ICU: Intensive care unit, APACHE II: Acute Physiology Assessment and Chronic Health Evaluation II.

les. Determined risk of the statistically significant variables for the development of nosocomial *Candida* infections was expressed as odds ratio (OR) and 95% confidence interval (CI) by multivariate logistic regression analysis. Data were expressed as mean ± standard error of mean (SEM) and percent (%) where appropriate. $p< 0.05$ was considered statistically significant.

RESULTS

NCI was diagnosed in 26 of 163 ICU patients (15.9%). Mean age of ICU patients was 65 ± 15 years, and female/male ratio was 8/18. There was no statistically significant difference between patients with or without *Candida* infections with regard to age, gender, underlying diseases, presence of a malignancy, APACHE II score and the leukocyte count (Table 1,2).

Isolation of *Candida* spp. via microbiological cultures among the specimens taken from 26 patients revealed positive results for *Candida albicans* in 13 patients (50%) and for *Candida* non-albicans in the other half (50%). *Candida* spp. in 26 patients were isolated from urine in 9 (34.6%) patients (second positive isolation after removing urinary catheter), trachea in 7 (26.9%) patients (all have tracheabronchial invasion but one was proved histologicaly), blood in 5 (19.2%) patients, oropharynx in 2 (7.6%) patients, and the skin in 1 (3.8%) patient. In 3 (11.5%) patients have more than three infectious loci were detected. We accepted five candidemias, seven tissue invasive *Candida* infections (one was proved by biopsy) and total 12 invasive *Candida* infections (five patients with blood culture positive + seven patients tracheabronchial tissue invasion), left 14 patients were accepted as very high risk of invasive *Candida* infections. Selected treatment for *Candida* infection was fluconazole alone in 13 (50.0%) patients and fluconazole unresponsive cases caspofungin acetate used in 12 (46.1%) patients (Table 3). Antifungal treatment was applied in 25 patients for an average duration of 3-52 days. Antifungal treatment was not administered in one patient because the diagnosis was made at the post-mortem by blood stream. Although empirical antibiotic treatment was selected in 146 patients (89.6%), it was summarized in Table 3.

Comparison of NCI positive and NCI negative patients in terms of invasive procedure frequency revealed that these procedures were applied to ICU patients with NCI positive more frequently when compared to patients with NCI negative (84.6% vs. 46.7% for mechanical ventilation; 73.1% vs. 18.2% for central venous cathete-

Table 3. Treatments of the patients with NCI in ICU.

NCI patients (n= 26)		**n (%)**
• Cultured species	*Candida albicans*	13 (50.0)
	Candida non-*albicans*	13 (50.0)
• Candida treatment	Fluconazole (Lumen)	13 (50.0)
	Fluconazole + caspofungin acetate (Cancidas)	12 (46.1)
All patients (n= 163)		**n (%)**
• Empirical antibiotic treatment		
Not applied		17 (10.4)
Applied		
Overall		146 (89.6)
Appropriate		81 (49.7)
Inappropriate		
	Brand	21 (12.9)
	Dose	19 (11.7)
	Use	42 (25.7)

* NCI: Nosocomial *Candida* infection, ICU: Intensive care unit.

rization; 76.9% vs. 23.4% for TPN; p< 0.001 for each). The ICU stay was found to be markedly longer in patients with NCI positive when compared to patients NCI negative (48.23 ± 7.5 days vs. 10.27 ± 0.83 days; p< 0.001). APACHE II scores were similar between patients with NCI positive and NCI negative (p> 0.05) (Table 2).

Regarding infections secondary to invasive procedures, catheter related infection (34.6% vs. 0.7%; p< 0.001), VAP (10.3% vs. 30.8%; p< 0.05) and VAT (15.3% vs. 73.1%; p< 0.001) were significantly more frequent among ICU patients NCI positive. Sepsis in terms of incidence (62.0% vs. 92.3%; p< 0.01) and recurrence rate (0.87 ± 0.08 vs. 3.54 ± 0.66; p< 0.001) were also more frequent in ICU patients with NCI positive. Moreover higher mortality rates were demonstrated in NCI positive (14.6% vs. 30.8%; p< 0.05) (Table 4).

According to multivariate analysis, OR ratio values, risk factors concerning development of nosocomial fungal infections were determined to be application of invasive procedures (mechanical ventilation, central venous catheterization, tracheostomy, TPN), infections due to invasive procedures (catheter site infection, VAT, VAP), and finally the multiple antibiotic use with at least three different brands, as summarized in Table 5.

Mortality rate due to NCI in ICU patients was found to be 30.8%. Mortality was shown to be increased with the risk factors established for NCI development. In that sense catheters (presence, number and duration), TPN (presence and duration), sepsis (presence and recurrence), and the use of multiple antibiotics were related with higher mortality rates. Isolation of non-albicans *Candida* spp. also correlates with increased mortality rates (10.7% vs. 17.9%; p< 0.05) in this study (Table 6).

DISCUSSION

In the present study conducted with non-neutropenic patients with or without *Candida* infections in a respiratory ICU, similarities between two groups of ICU patients with regard to gender, age, APACHE II scores and underlying conditions are compatible with the literature (9).

Table 4. Comparison of patients with/out NCI according to presence of infections, antibiotic treatment and prognosis*.

		NCI negative (n= 137)	NCI positive (n= 26)	Total (n= 163)
Catheter related infection	Absent	136 (99.3)	17 (65.4)	153 (93.9)
	Present	1 (0.7)	9 (34.6)*	10 (6.1)
Ventilator associated tracheobronchitis	Absent	116 (84.7)	7 (26.9)	123 (75.5)
	Present	21 (15.3)	19 (73.1)*	40 (24.5)
Ventilator associated peumonia	Absent	122 (89.7)	18 (69.2)	140 (86.4)
	Present	14 (10.3)	8 (30.8)$^{+}$	22 (13.6)
Sepsis	Absent	52 (38.0)	2 (7.7)	54 (33.1)
	Present	85 (62.0)	24 (92.3)^{q}	109 (66.9)
	Count	0.87 ± 0.08	3.54 ± 0.66*	1.31 ± 0.15
Antibiotic multitherapy	Double	0.93 ± 0.05	2.0 ± 0.39^{+}	1.09 ± 0.08
	Triple	0.21 ± 0.03	1.46 ± 0.31*	0.41 ± 0.06
Mortality	Absent	117 (85.4)	18 (69.2)	135 (82.8)
	Present	20 (14.6)	8 (30.8)$^{+}$	28 (17.2)

* Data are presented as n (%) or mean ± SD. $^{+}$p< 0.05; ^{q}p< 0.01; and *p< 0.001. Chi-square test for independent categorical variables and Student's t-test for mean scores were used for the analysis.
NCI: Nosocomial *Candida* infection.

Longer ICU stay in our patients with NCI positive was more prominent when compared to data obtained from ICU study in Istanbul-Turkey and recent new study conducted in a respiratory ICU study in Izmir-Turkey (48.2 days vs. 36.2; 22.3 days respectively) (14,15). But mortality rates were higher in those studies than our results (30.8% vs. 55.2; 55.3 respectively as above). Mortality attributable to *Candida* infections in our ICU (30.8%) seems to be moderate with respect to rates changing from 21-58% to 13-90% in the different studies done in other countries (16,17).

The increasing prevalence of *Candida* non-albicans species were reported in recent years (5,6,14,18-20). Although equally represented in our patients with NCI positive in ICU, *Candida*

Tablo 5. Risk factors for development of nosocomial *Candida* infections.

	p	OR	95%	CI
Invasive mechanical ventilation	**0.001**	6.27	2.05	19.16
Central venous catheter	**0.001**	28.3	4.61	32.04
Tracheostomy	**0.001**	8.23	3.2	20.7
Total parenteral nutrition	**0.001**	10.93	4.04	29.56
Multiple antibiotics	**0.001**	13.765	2.129	88.984
Catheter related infection	**0.001**	72	8.58	603.82
Ventilator associated tracheobronchitis	**0.001**	14.99	5.6	40.08
Ventilator associated pneumonia	**0.01**	3.87	1.42	10.52
Sepsis	**0.01**	7.34	1.66	32.35

Logistic regression analysis: OR: Odds ratio, CI: Confidence interval.

Table 6. Comparison of ICU mortality rates according to invasive procedures, length of ICU stay and APACHE score.

		Mortality negative (n= 135)	Mortality positive (n= 28)	Total (n= 163)
Catheter	Absent	72 (53.3)	5 (17.9)	77 (47.2)
	Present	63 (46.7)	23 (82.2)*	86 (52.8)
	Number	0.29 ± 0.05	1.11 ± 0.33^{+}	0.43 ± 0.07
	Duration (day)	4.19 ± 1.1	12.21 ± 3.8*	5.58 ± 1.1
Mechanical ventilation	Absent	72 (53.3)	5 (17.9)	77 (47.2)
	Present	63 (46.7)	23 (82.2)*	86 (52.8)
	Duration (hour)	107.13 ± 29.1	180.1 ± 48.4	119.6 ± 25.5
Tracheostomy	Absent	120 (87.6)	12 (46.2)	132 (81.0)
	Present	17 (12.4)	14 (53.8)*	31 (19.0)
Total parenteral nutrition	Absent	1056 (78.5)	5 (17.9)	111 (681)
	Present	29 (21.5)	23 (82.1)*	52 (31.9)
	Duration (day)	1.84 ± 0.4	8.26 ± 1.9^{q}	3.13 ± 0.5
Candida spp.	Albicans	10 (7.4)	3 (10.7%)	13 (8.0)
	Non-albicans^{+}	8 (5.9)	5 (17.9)	13 (8.0)
APACHE II score	Admission to RICU	18.08 ± 0.5	24.43 ± 1.2	19.18 ± 0.54

* Data are presented as n (%) or mean ± SEM. +p< 0.05; qp<0.01; and *p< 0.001. Chi-square test for independent categorical variables and Student's t-test for mean scores were used for the analysis.
ICU: Intensive care unit.

non-albicans (10.7%; 3/13) was shown to be related with more frequent mortality rates when compared to *C. albicans* (17.9%; 5/13) according to our results. This finding opposes mortality rates reported to be similar for *C. albicans* (61%; 22/36), and non-albicans (62%; 17/27) in a recent study, but similar in two Turkish studies (9,14,15).

In our case, risk factors concerning development of nosocomial fungal infections were multiple antibiotics use with at least from three different brands. This strongly supports the results of past studies in which use of broad-spectrum antibiotics, indwelling catheter, TPN, admission to the ICU, intravenous lines, haemofiltration procedures, adult respiratory distress syndrome, diabetes mellitus, malignancy, invasive mechanical ventilation, hospital-acquired bacterial infection, APACHE II score of 18 or higher and previous fungal colonisation were the predisposing risk factors for candidemia (9,17). APACHE II score of 18 or higher was reported to be a risk factor for the development of *Candida* infections ICU patients (21). Although non-significant APACHE II scores, were higher in patients with NCI positive than NCI negative (APACHE II score 21.2 vs. 18.7).

Representing the respiratory nature of our ICU, VAT was determined to be the most important risk factor for the development of NCI, with an OR of 14.9, followed by the use of multiple antibiotics. Previously shown interaction of VAT with the duration of mechanical ventilation and the length of the ICU stay suggests the influence of VAT in the development of fungal infections in RICU (22).

Anatomic site of colonization was defined to be effective in determining the risk factor status concerning nosocomial candidiasis but largely for patients with cancer and hematopoietic stem cell transplants. Most popular isolation sites in our patients were tracheal aspirations and the urine which were previously shown to be associated with the increased risk of developing *Candida* infection when to compare patients who were not colonized (23).

In contrast to past studies which lack of the relation between sepsis and mortality due to *Candida* infections, sepsis was found to be correlated with the increased mortality rates according to our results (24). Increased mortality in case of longer duration of catheters and TPN in the present study supports the fact that delayed removal of central lines may lead to poorer outcome in non-neutropenic patients with *Candida* infections (17). Also a new study from Turkey done by Turgut and co-workers, they founded *Candida* spp. was the most frequent pathogen of device associated infection in ICU in Denizli-Turkey (25).

Application of fungal treatment in all of our non-neutropenic patients with NCI positive supports the importance of the consensus obtained with regard to use of antifungal drugs safely in non-neutropenic ICU patients due to the introduction of new and less toxic antifungal agents over the last decade (26). However the observed shift towards non-albicans strains may indicate the contribution of treatment failure to the mortality rates. Recently a new concensus statement on the management of invasive candidiasis in ICUs in Asia-Pacific Region was published and it was suggested that after isolated yeast in blood, fluconazole is drug of choice if no recent antifungals, major organ dysfunction or acute crisis; otherwise drug of choise is caspofungin or micafungin (27).

As a result, isolation of non-albicans *Candida* spp. and the presence of determined risk factors for the development of nosocomial candidiasis indicate higher mortality rates in non-neutropenic respiratory ICU patients. In that sense catheters (presence, number and duration), TPN (presence and duration), sepsis (presence and recurrence), and the use of multiple antibiotics are related with the poorer outcome in ICU patients early identification of which may provide the selection of appropriate preventive and therapeutic measures for the nosocomial *Candida* infection.

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