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Antifungal susceptibility, risk factors and treatment outcomes of patients with candidemia at a university hospital in Saudi Arabia

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Abstract

Background: Candidemia is a major cause of morbidity and mortality in hospitalized patients. The spectrum of candidemia has been changed especially among critically ill patients due to emergence of non-*albicans Candida* (NAC) species. The increasing use of azole agents is suggested to be responsible for this epidemiological shift**.** NAC species are of special concern because of their high drug-resistance and increasing prevalence**.**The aim of this study was to detect antifungal-susceptibility patterns, treatment outcomes and associated risk factors in patients with candidemia who were admitted to King Abdulaziz University Hospital (KAUH), Jeddah, Kingdom of Saudi Arabia (KSA) .

Methods: This work represents a cross sectional study done in the Clinical and Microbiology Laboratory at KAUH, during the period from March 2012 till February 2014 on a total of 141 patients with candidemia. They were 31(22%) Saudi and 110(87%) non-Saudi patients with age ranged from 1 day - 102 years. Blood cultures were collected for suspected cases of candidemia, followed by subculture on SDA. Identification was done by VITEK MS (MALDI-TOF MS), and confirmation of *Candida* isolates and antifungal-susceptibility testing were performed by using VITEK ®2 system.

Results: *C.albicans* isolates accounted for 39.7%, followed by *C. tropicalis* (21.3%), *C. galabrata* (18.4%) and *C. parapsiliosis* (14.9%). Additionally, *C. dublinsis*, *C. krusei* and *C. famata* were representing 2.1%, 2.1% and 1.4%, respectively. All *Candida* isolates were 100% susceptible to amphotericin B. The best susceptibility to fluconazole was detected among each *C. dubliensis* and *C. famata* (100%). All *C. krusei* isolates were resistant to fluconazole, while they were susceptible

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to other antifungal agents. All isolates were susceptible to flucytosine, except *C. albicans* and *C. dubliensis* which were susceptible 92.9% and 66.7%, respectively. All isolates were susceptible to itraconazol, except *C. albicans* and *C. tropicalis* which were susceptible 94.6% and 96.7%, respectively. The percentage of deceased patients with candidemia was significantly higher than the survivors among age group >64 years, particularly those who were mechanically ventilated and those understeroid therapy. The percentage of deceased patients was significantly higher than survivors among those admitted to adult ICUs (73.78%vs 26.23%) .

Conclusion: This study shows an epidemiological shift to higher NAC species isolation rates, with 100% susceptibility to amphotericin B in all isolates either *C. albicans* or NAC species, and 100% susceptibility to fluconazole among *C. dubliensis* and *C. famata*. Patients aged > 64 years, admission to adult ICUs, mechanical ventilation and steroid therapy were significant risk factors for increased mortality due to candidemia.

Key Words: Candidemia, Non- albicans Candida, Antifungal susceptibility

Introduction

Candida is by far the most common fungal pathogen found in bloodstream [1]. The incidence of candidemia has been increasing worldwide. The epidemiology of candidemia has been changed in the past decades due to use of immunosuppressive and cancer therapy, AIDS epidemic, patients receiving transplantation and the increasing use of antibacterial drugs in hospital settings and even in the community[2]. Mucosal colonization by *Candida* species, indwelling vascular catheters as central venous catheters, total parenteral nutrition, steroid therapy, abdominal surgery, and immunocompromised condition are also associated risk factors for candidemia [3,4].

Candidemia is becoming a major cause of morbidity and mortality in hospitalized patients. The spectrum of candidemia has been changed especially among critically ill patients due to emergence of non-*albicans Candida* (NAC) species, including *C. tropicalis*, *C. parapsilosis, C. krusei*, and *C. glabrata.* The increasing use of azole agents is suggested to be responsible for this epidemiological shift [5,6].

NAC species are of special concern because of their high drug-resistance and increasing prevalence in invasive candidiasis [7]. Several years ago, different studies have been reported about candidemia in hospitals of Saudi Arabia, and these studies have used different designs, prospective vs. retrospective and different patient groups (ICU vs. non-ICU) [8-12].

The aim of this study was to detect antifungal-

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susceptibility patterns, treatment outcomes and associated risk factors in patients with candidemia who were admitted to King Abdulaziz University Hospital (KAUH), Jeddah, Kingdom of Saudi Arabia (KSA) .

Material and Methods

Study design and setting

A prospective cross-sectional study was done in the Clinical and Molecular Microbiology at KAUH from March 2012 through February 2014.

Candidemia was defined according to study of Leon *et al*, [13] as at least one positive blood culture from peripheral line for *Candida* spp. in patients with clinical features of infection.

Ethical consideration

The study was approval by Research Ethics Committee, the Unit of Biomedical Ethics, Faculty of Medicine, King Abdulaziz University (Reference Number: 830-12).

Subjects

This study was included 141 hospitalized patients who were admitted in different units of KAUH. Their ages ranged from 1 day to 102 years with mean ±sd (37.85±31.65) years, of these 63 (44.7%) were males and 78 (55.3%) females. They were 31 (22%) Saudis and 110 (78%) non-Saudis. Candidemia was diagnosed by isolation of *Candida spp*. from the blood culture of each patient.

Inclusion criteria

All candidemia cases which were considered as nosocomial infection included in the study by taking full patient's history and clinical examination, laboratory investigations, assessment of risk factors and underlying diseases. Candidemia cases referred from other hospitals or patients with second attack of candidemia were excluded from this study.

Methods

Blood cultures were performed using automated blood culture system (BacT/Alert, Organon, Teknika, USA).A total of 10mls of each patient's blood was inoculated into each bottle of blood culture system, one for aerobic and another for anaerobic growth. For pediatric patients, up to 5 mls of blood were inoculated into a single pediatric bottle. Culture bottles were loaded into BacT/Alert blood culture and kept until designated positive or for a maximum of 5 days incubation time. All bottles designated positive were smeared for Gram-stain. Culture bottles positive for yeast cells were subcultured on Sabouraud dextrose agar (SDA) (Saudi prepared media Laboratories, Riyadh, KSA) and the yeasts were identified with the use of VITEK MS at the same day if sufficient growth on SDA. The identification (ID) of *Candida* species is confirmed by using VITEK®2 system for ID and antifungal-susceptibility testing (bioMerieux, Inc., France) [14].

Yeast identification and anti-fungal susceptibility testing by VITEK-2

The isolated pure colonies were selected from SDA and a purity plate was done to ensure that a pure culture was used for testing. A total of 3 ml of 0.45% sterile saline were aseptically added into sterile plastic test tube. A sufficient number of morphologically similar colonies was transferred by a sterile loop to the saline tube and its density was checked by using Vitek 2 DensiCheck which should be equivalent to (2) McFarland then, the suspension tube was placed in the cassette followed by an empty tube and the card for identification of yeast was placed in the suspension tube and the card for AST (AST-YS07) was placed in the empty tube. When the sample cycle was finished, the cassettes and the tubes were discarded. Minimal inhibitory concentration (MIC) was calculated and represented as (sensitive, intermediate or resistant) [15].

Table 1. Demographic data of 141 patients with candidemia.

Item	No.(%)
Age groups	
< 1 year	40(28.4%)
1-18	11(7.8%)
19-49	28(19.9%)
50-64	27(19.1%)
>64	35(24.8%)
Sex	
Males	63(44.7%)
Females	78(55.3%)
Nationality	
Saudi	31(22.0%)
Non-Saudi	110(78.0%)
Wards	
Adult ICUs	61(43.2%)
Pediatric ICU	32(22.7%)
Adult wards	34(24.1%)
Pediatric wards	14(9.9%)
Outcome	
Deceased	85(60.3%)
Survived	56(39.7%)

Statistical analysis

Data were analyzed using Statistical Package for Social Sciences (SPSS) software, version 18. Chi-square test was utilized to test for the association and/or difference between categorical variables. Yates's correction was applied when appropriate. Odds ratio and 95% confidence interval were calculated. Continuous variables were presented as mean, standard deviation and range. P value less than 0.05 was considered statistically significant.

Results

Demographic data of the 141 patients with candidemia are presented in **Table (1)**. There were 31(22%) Saudis, and 110(78%) non-Saudis. A total of 85(60.3%) patients were deceased following candidemia. High rates of patients were aged < 1 year (40; 28.4%) or aged >64 (35;24.8%). A total of (85; 60.3%) patients were deceased following candidemia **(Table 1)**. *C. albicans* was the most

Table 2. Species distribution and susceptibility patterns of *Candida* isolates to anti-fungal drugs.

Candida species (no/%)	% susceptible to Amphotericin-B	% susceptible to Fluconazole	% susceptible to Flucytosine	% susceptible to Itraconazole
C. albicans (56/39.7)	100	94.6	92.9	94.6
C. galabrata (26/18.4)	100	92.3	100	100
C. tropicalis (30/21.3)	100	96.7	100	96.7
C. parapsiliosis (21/14.9)	100	95.2	100	100
C. dublinsis (3/2.1)	100	100	66.7	100
C. krusi (3/2.1)	100	0.0	100	100
C. famata (2/1.4)	100	100	100	100
Total no.(141)	141(100%)	131(92.9%)	136(96.5%)	137(97.2%)

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common species detected (39.7%), followed by *C. tropicalis* (21.3%), *C. galabrata* (18.4%) and *C. parapsiliosis* (14.9%). However, *C. dublinsis*, *C. krusei* and *C. famata* were represented by 2.1%, 2.1% and 96.7% susceptible, respectively **(Table 2).**

All *Candida* isolates were 100% susceptible to amphotericin B. The best susceptibility to fluconazole was detected among *C. dubliensis* and *C.famata* (100%). *C. krusei* isolates were 100% resistant to fluconazole, but these were 100% susceptible to other antifungal agents. All isolates were susceptible to flucytosine, except *C. albicans* and *C. dubliensis* which were 92.9% and 66.7% susceptible, respectively. All isolates were susceptible to itraconazole, except *C. albicans* and *C. tropicalis* which were 94.6% and 96.7% susceptible, respectively. **(Table 2)**.

The percentage of deceased patients was significantly higher among those who were mechanically ventilated (72.6% vs 27.4%), and who received steroid therapy than others (90.9% vs 9.1%). There was an increased risk of mortality in candidemic patients who were under dialysis, have CVC, chronic renal impairment, heart diseases, diabetes mellitus and those with long stay in hospital (>20 days) or infected/colonized with Candida **(Table 3)**. The percentage of deceased

Table 3. Risk factors, underlying diseases and their effects on the outcome of candidemia patients

Patients (total: 141)	Deceased N=85	Survived N=56	x2	p-value	OR 95%CI
Risk factors					
1-CVC; 103(73%)	66(64.08%)	37(35.9%)	2.3	0.12	1.78(0.79-4.05)
2-Urinary catheter; 101(71.6%)	58(57.4%)	43(42.6%)	1.21	0.27	0.65(0.25-1.5)
3-M.V; 95(67.4%)	69(72.6%)	25 (27.4%)	17.5	0.001**	4.68(4.68-10.6)
4-TPN; 47(33.3%)	23(48.9%)	24(51.1%)	3.79	0.051	0.49(0.23-1.07)
5-Anti-bacterials; 95(67.4%)	58(61.05%)	37(38.95%)	0.07	0.78	1.11(0.51-2.40)
6-Steroid therapy; 22(15.6%)	20(90.9%)	2(9.1%)	10.2	0.001**	8.31(1.75-53.1)
7-Prematurity; 11(7.8%)	5(45.45%)	6(54.55%)	2.11	0.14	0.41(0.10-1.63)
8-Dialysis; 21(14.9%)	15(71.43%)	6(28.57%)	1.28	0.25	1.79(0.59-5.58)
9-Liver impairment; 20(14.2%)	14(70.0%)	6(30.0%)	0.27	0.60	1.31(0.43-4.2)
10-Candiduria ; 32(22.7%)	24(75.0%)	8(25.0%)	3.74	0.052	2.36(0.91-6.31)
11-Candida in tracheal aspirate; 36(25.5%)	26(72.2%)	10(27.8%)	2.85	0.089	2.03(0.83-5.03)
12-length of hospital stay before candidemia; (23.82±18.34 days,range,1-84)					
Underlaying diseases					
1-Chronic Renal Impairment; 9(6.4 %)	7(77.8%)	2(22.2%)	0.70	0.40	1.97(0.35-14.3)
2-Chronic Liver Disease; 3(2.1%)	2(66.7%)	1(33.3%)	0.05	0.81	1.33(0.09-37)
3-Solid Malignancy; 20(14.2%)	12(60.0%)	8(40.0%)	0.001	0.97	0.99(0.34-2.88)
4-Hematological Malignancy; 5(3.5%)	3(60.0%)	2(40.0%)	0.001	0.97	0.98(0.13-8.6)
5-Chemotherapy; 5(3.5%)	3(60.0%)	2(40.0%)	0.001	0.97	0.98(0.13-8.6)
6-Respiratory Diseases; 12(8.5%)	7(58.3%)	5(41.6%)	0.02	0.88	0.92(0.24-3.5)
7-Heart diseases; 10(7.1%)	7(70.0%)	3(30.0%)	0.42	0.51	1.59(0.35-8.15)
8-Human Immunodeficiency Virus;2(1.4%)	2(100.0%)	0.0(0.0%)	1.43	0.24	----------
9-Diabetes Mellitus; 29(20.6%)	20(68.96%)	9(31.04%)	1.04	0.30	1.57(0.61-4.13)
10-Intestinal Obstruction; 4(2.8%)	0.0(0.0%)	4(100.0%)	6.25	0.015*	----------
11-Stroke; 1(0.7%)	0.0(0.0%)	1(100.0%)	1.52	0.21	----------

*Significant; **Highly Significant; OR: Odds ratio; CI: Confidance interval

patients was significantly higher in patients aged ≥ 64 years than younger ages (76.9% vs 23.07%) **(Table 4)**.

The percentage of deceased patients in adult ICU was significantly higher than the survivors (73.78% vs 26.23%) **(Table 4)**. There were no significant differences between deceased and survived candidemia patients infected with different *Candida* species **(Table 5)**.

Discussion

Candida bloodstream infection (CBSI) represents an important problem in critically ill hospitalized patients. (CBSI) is often a consequence of long term use of broad-spectrum antibacterial therapy, complex surgical procedures and invasive medical devices. The epidemiology of candidemia is changing with an increase in the proportion of NAC [16].

Table 4. Details of risk factors associated with the outcome of 141 candidemia cases

Patients	Deceased No.(85;60.3%)	Survived No. (56;39.7%)	x2	p-value	OR 95%CI
Age group (no)					
< 1 year (40)	23(57.5%)	17(42.5%)	0.03	0.85	1.7(0.48-2.37)
1-18 (11)	4(36.36%)	7(63.64%)	2.85	0.91	0.35(0.08-1.41)
19-49 (28)	14(50.0%)	14(50.0%)	1.54	0.21	0.59(0.24-1.47)
50-64 (27)	18(66.7%)	9(33.3%)	0.57	0.45	1.4(0.54-3.7)
>64 (39)	30(76.9%)	9(23.07%)	6.23	0.015*	2.85(1.15-7.22)
Sex					
Males (63)	42(66.7%)	21(33.3%)	1.94	0.16	1.63(0.77-3.44)
Females (78)	43(55.1%)	35(44.9%)	1.94	0.16	0.6(0.29-1.29)
Nationality					
Saudi (31)	21(67.7%)	10(32.3%)	0.92	0.33	1.51(0.6-3.82)
Non Saudi (110)	64(58.2%)	46(41.8%)	0.92	0.33	0.66(0.26-1.65)
Ward					
Adult ICU; 61 (43.2%)	45(73.78%)	16(26.23%)	2.81	0.004**	2.81(1.29-6.17)
Pediatric ICU; 32 (22.7%)	21(65.6%)	11(34.4%)	0.42	0.51	1.31(0.54-3.25)
Adult ward; 34(24.11%)	15(44.1%)	19(55.89%)	2.64	0.10	0.53(0.23-1.22)
Pediatric ward; 14 (9.9%)	4(28.6%)	10(71.4%)	6.53	0.012*	0.23(0.06-0.85)
Length of stay					
From 1-5 days; 20(14.2%)	9(45.0%)	11(55.5%)	2.27	0.13	0.48(0.17-1.33)
From 6-10 days; 17(12.1%)	6(35.3%)	11(64.7%)	5.04	0.02*	0.31(0.09-0.99)
From 11-15 days; 19(13.5%)	14(73.7%)	5(26.3%)	1.65	0.19	2.01(0.62-6.8)
From 16-20 days; 24(17%)	14(58.3%)	10(41.7%)	0.05	0.83	0.91(0.34-2.42)
More than 20 days; 61(43.3%)	42(68. 9%)	19(31.1%)	2.43	0.11	1.85(0.87-3.96)

*Significant; **Highly significant; OR: Odds ratio; CI: Confidance interval.

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Table 5. Outcome of patients with candidemia according to *Candida* species

Species (no.)	Deceased No.(%)	Survived No.(%)	x2	p-value	OR 95%CI
C. albicans (56)	36(64.3)	20(35.7)	1.04	0.36	1.44(0.67-3.08)
C. tropicalis (30)	20(66.7)	10(33.3	0.42	0.42	1.42(0.56-3.6)
C. galabrata (26)	14(53.8)	12(46.2	0.74	0.49	0.74(0.29-1.91)
C. parapsiliosis (21)	10(47.6)	11(52.4)	0.19	1.65	0.55(0.19-1.52)
C. dublinsis (3)	2(66.7)	1(33.3)	0.05	0.81	1.33(0.09-37.88)
C. Krusei (3)	2(66.7)	1(33.3)	0.05	0.81	1.33(0.09-37.88)
C. famata (2)	1(50)	1(50)	0.09	0.76	0.65(0.02-24.5)

During the current study; overall mortality associated with candidemia was 60.3 % **(Table 1).** Other researchers reported similar results to our with overall crude mortality among their patients with invasive candidiasis or candidemia in the range of 40 - 60% [17-19]. A previous Saudi study reported that approximately two-fifths (40.6%) of the patients died within 30-days after isolation of *Candida* species from their sterile body sites [20]. Kumar *et al*. [21] in Pakistan, reported lower mortality rate (23.4%) in their study [21], and Playford *et al.* [22], reported higher mortality rate associated with candidemia due to NAC (80%) among non-neutropenic critically ill patients admitted to ICU.

This current study showed that *C. albicans* was the predominant isolate in patients with candidemia (39.7%), while all other *Candida* species (NAC) were responsible for 60.3% of the cases, and the most common NAC species was *C. tropicalis* (21.3%) among all isolates (Table2). However, an earlier study done by Akbar and Tahawi [9] at the same hospital (KAUH) reported that *C. albicans* was the most frequently isolated species (71%), followed by *C. tropicalis* (13%) and *C. parapsilosis* (13%).Both studies showed that the most common species was C. *albicans* , followed by *C. tropicalis*, whereas the study of Bukharie *et a*l [8] in Saudi Arabia, has found that *C. albicans* caused 19% of candidemia cases .

Al- Thaqafi *et a*l. [23],demonstrated that the total number of candidemia cases at King Abdulaziz Medical City (KAMC) in Jeddah during an 8-year period (2002 -2009) was relatively higher than previously reported data from other regions of Saudi Arabia .

Eksi *et al*. [24] in Turkey, found that 47.7% of their isolates from candidemia cases were *C. albicans*, followed by *C. parapsilosis* (36.9%) and other *Candida* species represented by 15.4%. Chi *et al.* [7] in Taiwan, reported that *C. albicans* represented 43.5%, meanwhile, non-*albicans* spp. including *C.glabrata*, *C.tropicalis*, C. *parapsilosis*, *C.krusei*and*C. heamulonii* were responsible for (56.5%) of candidemia cases [7]. Montagna *et al*. [13] in Italy, reported that 59.8 % of their studied candidemia cases were caused by NAC, and *C. parapsilosis* was the most common species. Also, the study of De Luca *et al.* [25]in Italy, found that *C. albicans* represented 48% of isolates in candidemia cases, while all other NAC was represented by 52% and the most common species was *C. glabrata*. The highest prevalence of NAC was found by Kumar *et al*. [21] in Pakistan, where NAC species were isolated in 90.9% of candidemic patients including *C. parapsilosis* (36.4%), *C. lusitaniae* (29.9%), *C. tropicalis* (20.8%), *C. glabrata* (3.9%), and only 7 patients (9.1%) were having *C. albicans*. This finding showed that *C. albicans* is less common in certain countries than others and there is an etiological shift to higher isolation of NAC species in most candidemic patients which has been also observed in our study.

Antifungal susceptibility is highly important for management of patients with candidemia. The results of this study showed that all isolated *Candida* species were susceptible to amphotericin B, which is in agreement with the results of many other studies [24-25]. However, the increased usage of antifungal agents may contribute to increased occurrence of resistance in some *Candida* species more than others [26].

In general, our antifungal susceptibility results were comparable to that reported by Pfllar *et al.*, [27], their study observed that fluconazole-resistance was extremely rare (1%) among blood isolates of *C. albicans*, *C. tropicalis, C. parapsilosis*, while *C. lusitaniae* and *C. glabrata* exhibited 2% and 8% resistance to fluconazole, respectively.

Al Thaqafi *et al.* [23] in Saudi Arabia, found that fluconazole-susceptibility was 38.5% for *C. albicans* and 52.5% for other *Candida* species, while an Egyptian study of Mohtady *et al.* [28] reported that fluconazole-resistant *C. dubliniensis* and *C. albicans* were (55.6%) and (49%), respectively. Omrani *et al.*,[20], found that more than 90% of *C.albicans, C. parapsilosis*, and *C. tropicalis* isolates in their study were susceptible to fluconazole and caspofungin. Moreover, the vast majority of *Candida* isolates were susceptible to voriconazole and amphotericin B, while 33.3% of *C. krusei* isolates were resistant to caspofungin. These data were comparable to our results, especially that all *Candida* isolates in this study were susceptible to voriconazole and caspofungin.

In agreement with our overall results, De Luca *et al.* [25], has found that all *Candida* species were susceptible to amphotericin B, whereas *C. albicans* and *C. parapsilosis* susceptibility to fluconazole was 100%, with decreased susceptibility of *C. glabrata* to 76.5%. In addition, Ajenjo*et al.* [29], indicated that 88.8% of their *Candida spp.* isolates were fluconazole-susceptible.

The increase incidence of *Candida* infections contribute to increased usage of antifungal and more developing of resistance in *Candida* species [26]. Therefore, early and adequate empirical anti-fungal treatment plus early removal of central catheters are considered the main factors to reduce use of antifungal drugs, morbidity and mortality. It is necessary to implement guidelines of empirical antifungal treatment in patients with highly risk factors of developing candidemia [30].

The role of intravascular catheters in causing candidemia has been documented. Removal of vascular catheters has been advocated as an adjunctive strategy for treating patients with catheter-related candidemia [31]. This study showed that most patients (73%) with central venous catheters (CVCs) and those who received antibacterials (67.4%) had developed candidemia **(Table 3)**. A previous study done at the same hospital by Akbar and Tahawi [9], found that patients with CVCs (77%) who received broad-spectrum antibacterial therapy (87%) were associated with candidemia. The study of Chander *et a*l. [6], has similar results to ours regarding associated risk factors with candidemia.

Other associated risk factors for candidemia observed in this study included; age < 1 year > 64 years, urinary catheter, mechanical ventilation, undergoing dialysis, steroid therapy, and prolonged hospital stay for >20 days as shown in **Table 3 & 4.** The study of Montagna *et al.* [16], reported similar risk factors in their patients especially due to using of Hickman catheter and length of stay in ICU.

The present study shows that the incidence of *C. albicans* and *C. glabrata* was is higher among patients with solid compared to hematological malignancies, while the incidence of other *non-albicans Candida* species was also higher among patients with hematological than solid malignancies. Al-Thaqafi, *et al.*[23], reported in their study of over 8-year-duration at King Abdulaziz Medical City, Jeddah, that malignancy was significantly associated with the development of non-*albicans Candida* species.

The study of Kontoyiannis *et al.*[32], concluded that immunocompromised patients including those affected by solid tumors or haematological malignancies are at high risk for

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developing *Candida* infection. Additionally, the widespread use of fluconazole prophylaxis in haematological and stem cell transplant settings might be responsible for a decreased incidence of invasive *Candida* infections in these populations.

This study found that the rate of deceased patients was higher than Survived ones to candidemia with *C. albicans* (64.3% vs 35.7%) or NAC (57.6% vs 42.4%), with no significant differences between the two groups **(Table 5).** However, a study in Greece, found the overall mortality to be significantly higher in patients with NAC species than *C. albicans* associated with bloodstream infections (90% vs 52.8%) [33]. Kelvay et al.[34], recorded that mortality associated with *C. albicans* and *C. glabrata* candidaemia was 44% and 41%, respectively. Other studies reported higher rates of mortality in association with NAC species, especially *C. krusei, C. glabrata*and *C. tropicalis* [35-38].

This study concludes that there is an epidemiological shift to higher isolation of NAC species in candidemic patients and all *Candida* and NAC isolates were susceptible to amphotericin B. Additionally, increased mortality was observed in patients older than 64 years, with steroid therapy, mechanical ventilation and those who admitted to adult ICU.

Conflict of interest

None.

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