Distribution of *Candida species* among bloodstream isolates

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ABSTRACT

Objective: To identify the distribution of *Candida species* causing bloodstream infections.

Methods: This study was conducted at the Armed Forces Hospital, Riyadh, Kingdom of Saudi Arabia. All cases of candidemia from the period 1996 through to 2002 were retrospectively identified through the records from the Department of Clinical Microbiology.

Results: Two hundred and ninety-four candidemic episodes were identified, 176 (59.9%) occurred in the intensive care units (ICUs), 32 (10.9%) medical, 30 (10.2%) surgical wards, 24 (8%) from patients with hematologic malignancies and 15 (5%) from pediatric wards. *Candida albicans* (*C. albicans*) was the most frequently isolated species with 149 (50.7%) cases, followed by *Candida tropicalis* (*C. tropicalis*) 61 (20.7%), *Candida parapsilosis* 32 (10.9%), *Candida krusei* (*C. krusei*) 23 (7.8%) and *Candida glabrata* 21 (7.1%). Other species were not common. There is an increase in the proportion of non *C. albicans species* as the causative agents of candidemia. In certain clinical settings, non *C. albicans species* predominate as in the Adult General Intensive Care Unit with *C. tropicalis* as the most common. While in patients with hematologic malignancies, *C. krusei species* is the most common.

Conclusion: These findings reinforce the need for continued and active surveillance programs to address the changes in the species distribution among candidal bloodstream isolates which will help to develop effective, preventive and therapeutic strategies.

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Candidal bloodstream infections (CBSIs) increased dramatically over the past 2 decades. They currently represent the fourth most common nosocomial bloodstream infections.[1] Systemic *Candida* infections are associated with a high mortality rate (38%) and a prolonged hospital stay.[2] Previous studies have suggested that possible risk factors for CBSIs may include receipt of antibiotic agents, chemotherapy or steroids as with the presence of intravascular catheters, receipt of parental nutrition, surgery, hospitalization in intensive care units (ICUs), malignancy, neutropenia and prior fungal colonization.[3-5] *Candida albicans* account for approximately 50-60% of all nosocomial *Candida* infections, although a noticeable shift towards *Candida species* other than *C. albicans* has been observed.[6-10] This is important considering the intrinsic or acquired antifungal resistance in several of these species.[10,11] Therefore, species directed therapy should be administered for fungemia according to the species identified and its antifungal susceptibility pattern.

Methods. The laboratory data base was used to identify all *Candida species* recovered from blood cultures between 1996 through to 2002 at the Armed Forces Hospital, Riyadh, Kingdom of Saudi Arabia (KSA) which is a tertiary hospital with a 1200 bed capacity.

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Table 1 - Species distribution of *Candida* bloodstream distribution isolates by location.

Candida species	ICUs		Hem		Surg		Med		Ped		Renal		Onc	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
C. albicans	88	(29.9)	7	(2.4)	18	(6.1)	16	(5.4)	9	(3.1)	8	(2.7)	3	(1)
C. tropicalis	42	(14.3)	6	(2)	3	(1)	7	(2.4)	2	(0.7)	1	(0.3)	-	-
C. parapsilosis	18	(6.1)	2	(0.7)	6	(2)	2	(0.7)	3	(1)	1	(0.3)	-	-
C. krusei	10	(3.4)	8	(2.7)	2	(0.7)	2	(0.7)	-	-	-	-	1	(0.3)
C. glabrata	13	(4.4)	-	-	1	(0.3)	4	(1.3)	1	(0.3)	2	(0.7)	-	-
C. famata	2	(0.7)	1	(0.3)	-	-	-	-	-	-	-	-	-	-
C. species	3	(1)	-	-	-	-	1	(0.3)	-	-	1	(0.3)	-	-

C - Candida, ICUs - intensive care units, Hem - hematology ward, Surg - surgical wards, Med - medical wards, Ped - pediatric wards, Renal - renal dialysis and transplant ward, Onc - oncology ward.

Demographic data includes age, gender and hospital unit. Intensive care units were categorized as follows: adults general ICU (AGICU), pediatric general ICU (PGICU), adult cardiac ICU (ACICU), pediatric cardiac ICU (PCICU) and neonatal ICU (NICU). Both AGICU and PGICU are combined medical, surgical, burn and trauma ICUs. Blood cultures were performed using the automated blood culture system [BACTEC 9240, Beckton Dickinson, United States of America (USA)]. Ten ml of patient blood was inoculated into each bottle of blood culture one for aerobic and the other for anaerobic growth. Culture bottles were loaded into the instrument and remained there for 7 days or until designated positive. All bottles designated positive were smeared for gram stain, culture bottles positive for yeast cells were cultured onto sabouraud agar and CHROM agar *Candida* (CHROM agar, Microbiology, Paris, France). The yeast were identified with the use of germ tube reaction, colony morphology and color reaction on CHROM agar, and commercial identification system API 20C (Analytab products, plain view, NY, USA). Antifungal susceptibility testing was not carried out as it was not yet available in our laboratory.

Results. The total number of positive blood cultures during this period was 7,347. *Candida species* constituted 294 (4%) of all the isolates. Each strain represented by a unique isolate from a patient. There were 164 males and 130 females and the age ranges from 2-weeks to 100-years. One hundred and seventy six (59.9%) episodes were from patients in the ICUs while 32(10.9%) were from the medical wards, 30 (10.2%) from the surgical wards, 24 (8.2%) from patients with hematologic malignancies, 15 (5.1%) from pediatric ward, 13 (4.4%) from renal dialysis and transplant patients and 4 (1.4%) from oncology ward. Among ICU categories, candidemia commonly occur in AGICU 57 (19.4%), followed by PCICU 48 (16.3%) PGICU 36 (12.3%), ACICU 18 (6.1%) and NICU 17 (5.8%). The frequency of bloodstream infections (BSIs) due to different *candida species* was as follows: *C. albicans* accounted for 149 (50.7%) of all CBSIs while non *C. albicans species* were responsible for 145 (49.3%) of cases. Among the non *C. albicans species*, *C. tropicals* accounted for 61 (20.7%) of cases followed by *C. parapsilosis* 32 (10.9%), *C. krusei* 23 (7.8%), *C. glabrata* 21 (7.1%) while uncommon *Candida species* 5 (1.7%).

Table 1 shows species distribution of CBSIs isolates by location. The following were the most commonly isolated *candida species* in ICUs generally: *C. albicans* 88 (29.9%), *C. tropicalis* 42 (4.3%), *C. parapsilosis* 18 (6.1%) and *C. glabrata* 13 (4.4%). In AGICU, *C. tropicalis* were the most common non *C. albicans species* 14 (4.8%) followed by *C. glabrata* 10 (3.4%) and *C. krusei* 7 (2.4%) while in NICU the most common non *C. albicans species* was *C. parapsilosis* (**Table 2**). In patients with hematologic malignancies, the distribution was as follows: *C. krusei* 8 (2.7%), *C. albicans* 7 (2.4%), *C. tropicalis* 6 (2%) and *C. parapsilosis* 2 (0.7%).

Discussion. Numerous studies have documented the increased incidence of candidal bloodstream infection in recent decades.[1,4,13] The most recent analysis of data from SENTRY report confirms the fact that *Candida species* remain the fourth most common cause of nosocomial bloodstream infection (BSI).[1] However, our data showed that *Candida species* are the sixth leading

Table 2 - Distribution of *Candida species* among intensive care unit categories.

C. Species	Intensive care units									
	AGICU		PGICU		ACICU		PCICU		NICU	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
C. albicans	21	(7.1)	17	(5.8)	12	(4.1)	2.5	(8.5)	13	(4.4)
C. tropicalis	14	(4.8)	13	(4.4)	4	(1.4)	10	(3.4)	1	(0.3)
C. parapsilosis	3	(1)	5	(1.7)	-	-	7	(2.4)	3	(1)
C. krusei	7	(2.4)	1	(0.3)	2	(0.7)	-	-	-	-
C. glabrata	10	(3.4)	-	-	-	-	3	(1)	-	-
C. famata	-	-	-	-	-	-	2	(0.7)	-	-
C. species	2	(0.7)	-	-	-	-	1	(0.3)	-	-

C - Candida, ICUs - intensive care units, AGICU - adult general ICU, PGICU - pediatric general ICU, ACICU - adult cardiac ICU, PCICU - pediatric cardiac ICU, NICU - neonatal ICU.

cause of BSI hospital wide which may reflect an institutional variation.

Most of our candidemic episodes occur in high risk, critical care units where *Candida species* represent the fourth most common cause of BSI as reported by other studies.[12,13] Several factors may have contributed to this increase in candidemia in ICU settings. Intensive care unit stay with its associated invasive procedures especially central venous catheter, constituted an important risk factor of candidemia.[4,5,14.] Other risk factors include severity of illness which promotes yeast overgrowth[15] and disturbance of normal gut flora caused by the increased use of potent broad spectrum antibiotics.[16] The differences in frequency and species distributions between different types of ICUs may reflect the characteristics present among patients in each type of ICU and the variability of known risk factors for candidemia.[13] Although, *C. albicans* remains the most frequent cause of CBSIs in this study (50.7%), there is an increasing proportion of non *C. albicans species* as agents of candidemia (49.2%) which is consistent with both American and European multicenter investigations and other reports from KSA.[1,6-8,12,13]

Candida tropicalis has been known to sometimes be a major cause of candidemia. Although, numerous reports in neutropenic and non neutropenic patients have documented *C. tropicalis* as the most common non *C. albicans species*, the most recent SENTRY data showed that *C. tropicalis* is the third most common non *C. albicans species*.[1] In terms of patient group affected, *C. tropicalis* is seen more frequently in cancer patients than in surgical and ICU patients.[17] Our data shows that *C. tropicalis* is the most common non *C. albicans species* which agrees with the study carried out by Al-Hedaithy.[6] In our institution, it occurs mainly in ICUs. These findings may be attributed to different patient categories admitted to ICUs.

Recent studies from Latin America, Canada and Europe show an overall increasing incidence of *C. parapsilosis* as an agent of fungemia.[1] It is now the most common non *C. albicans species* in some centers worldwide and in KSA.[1,8,18] It occurs mainly in non cancer patients particularly children and this frequent isolation may reflect suboptimal catheter care and infection control.[18] In our center, *C. parapsilosis* is the second non *C. albicans species* seen commonly in ICU patients with the highest proportion from pediatric ICUs and NICU. *Candida krusei* is an emerging non *C. albicans species*, with a particular predilection for neutropenic adult cancer patients. *Candida krusei* appears to be increasing in some reports and an association with fluconazole usage was observed.[19,20] This study shows also an increase in *C. krusei* fungemia occurring mainly in patients in adult ICUs and hematologic malignancies ward.

The recent data from the SENTRY program showed that *C. glabrata* was the most common non *C. albicans species* in the USA and its prominence may be influenced by extensive utilization of fluconazole at a relatively low doses (<400 mg/day), enhancing selection of this species.[1,21] This study shows that *C. glabrata* is the fourth non *C. albicans* isolated with highest frequency in AGICU patients. Other non *C. albicans species* were uncommon. Three cases of candidemia were due to *C. famata*, 2 cases occur in PCICU and one case in patient with hematologic malignancy.

Limitations of this study includes the lack of detailed clinical information of individual patients, detailed risk factors, antibiotic therapy and fluconazole use in different hospital settings which devoid us from performing analyses comparing different risk factors with changes in distribution of *Candida species*. Although routine antifungal susceptibility testing of all clinical specimens is not recommended, considering its existent limitations, periodic determination of antifungal susceptibility patterns is important in every institution especially those dealing with high risk patients where antifungal therapy is common.

In conclusion, this study highlights the importance of candidemia among hospitalized patients in our center. It emphasizes the need for continued surveillance to document changes in its species distribution and also the need for antifungal susceptibility testing which is of great clinical and therapeutic importance.

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