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190. Epidemiology and Risk Factors for Antifungal Resistance in Patients with Candidemia

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Background. *Candida* is a common nosocomial blood pathogen associated with high mortality. Data on antifungal resistance from Saudi Arabia is scarce. The objective of this study is to examine epidemiology, risk factors for antifungal resistance, and outcome among patients with candidemia.

Methods. A retrospective study conducted at King Faisal Specialist Hospital and Research Center-Jeddah branch (KFSHRC-J) The study included all patients 18 years and older with positive blood culture for candida over a 5-year period (2012–2016).

Results. We identified 92 cases of candidemia. The mean age was 59 years SD (18). *Candida galabrata* was the most prominent species 33 (36%) followed by *Candida parapsilosis* 22 (24%), *Candida albicans* 20 (22%), *Candida tropicalis* 13 (14%), *Candida krusei* 2 (2%), and others 2 (2%).

Resistance to fluconazole was identified in 14 (15%) cases, four of them were also resistance to voriconazole. Among cases resistance to fluconazole, seven (50%) cases were *C. parapsilosis*, two (14%) of each *C. galabrata*, *C. krusei*, and *C. Albicans* and one (7%) was *C. tropicalis*. In univariate analysis, previous exposure to echinocandin and mechanical ventilation within 3 months were associated with fluconazole resistance candidemia (12(15%) vs 7(50%), ($P = 0.007$), 28(36%) vs 10(71%), ($P = 0.014$), respectively). Patients with fluconazole resistance candida had a longer length of intensive care unit stay (median 26 days (IQR 6–40) days and 12 days (IQR 7–36)), respectively. Length of hospital stay was longer in patients with fluconazole resistance compared with nonresistance (median 83 days (IQR 29–199 days) and (31 days (IQR 17–75)), respectively. Thirty-day mortality of patients fluconazole resistance compared with non-resistance cases was not significant 43 and 55%, respectively ($P = 0.28$).

Conclusion. In our cohort, *Candida galabrata* is the most common species causing candidemia. Increasing fluconazole resistance candida parapsilosis is alarming. More regional epidemiological antifungal resistance studies are required to confirm this finding.

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191. Improved Survival of *Candida* CLABSI by Adherence to Standard of Care and Involvement of Infectious Diseases Consultant: A 5-Year Experience in a Single Academic Center

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Thursday, October 5, 2017: 12:30 PM

Background. Candidemia is the fourth most common nosocomial blood stream infection with significant morbidity and mortality. Central lines have been considered a risk factor for invasive fungal infection. We evaluated the epidemiology, management, and outcomes of *Candida* CLABSI in an academic medical center.

Methods. We conducted a retrospective cohort study in a single academic center from January 1, 2011 to December 31, 2016 of patients who had positive blood cultures for *Candida* sp. and met CDC criteria for CLABSI. Outcomes measured were 30-day mortality and relapse or recurrence. Descriptive statistics were used to compare the outcomes of patients who had infectious diseases consult and managed per standard of care (SOC) as defined by IDSA guidelines and those without.

Results. Of 722 CLABSI cases, 82 (11%) were due to *Candida* sp. *Candida* species isolated were as follows: *C. glabrata* (40%), *C. albicans* (32%), *C. parapsilosis* (9%), and others (19%). Median age of pediatric patients was 2.25 years (range 0.5–6) and median age of adults was 59 years (19–92). Most common comorbidities were malignancy (35%) and end-stage renal disease (21%). Non-tunneled catheters were present in 58% of cases. Median time from line placement to candidemia was 15 days (IQR 8–29). Sepsis was present in 34 (42%) cases. Seventy-four (90%) cases were initiated on antifungal therapy (AFT) when culture turned positive. After *Candida* speciation, AFT was adjusted appropriately for 82 (100%) cases. IDC was present in 56 (68%), of which 41 (73%) followed SOC, whereas 15 (27%) did not. Two of 26 patients (8%) without IDC received SOC. Complications occurred in 11/82 (13%) (three endocarditis, two osteomyelitis, three endophthalmitis, and four septic thrombophlebitis). Cure was achieved in 26/82 (32%). Relapse or recurrence occurred in 15/82 (18%). The 30-day mortality for the cohort was 50%. Patients with IDC who received SOC had lower mortality compared with those who did not (35% vs. 67%, respectively; $P = 0.03$).

Conclusion. *Candida* CLABSI was infrequent but had significant mortality in our cohort. Our results suggest that adherence to SOC per IDSA guidelines and involvement of IDC may improve survival of patients with *Candida* CLABSI. Future studies are needed to validate these findings.

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192. Treatment Bundle Improves Outcomes in the Management of Candidemia at Large Urban Academic Medical Center

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Session: 44. Clinical Mycology

Thursday, October 5, 2017: 12:30 PM

Background. A candidemia treatment bundle (CTB) may increase adherence to guideline recommended candidemia management and improve patient outcomes. The purpose of this study was to evaluate the impact of a best practice alert (BPA) and order-set on optimizing compliance with all CTB components and patient outcomes.

Methods. A single center, pre-/post-intervention study was completed at Grady Health System from August 2015 to August 2017. Post-CTB intervention began August 2016. The CTB included a BPA that fires for blood cultures positive for any *Candida* species to treatment clinicians upon opening the patient's electronic health record. The BPA included a linked order-set based on treatment recommendations including: infectious diseases (ID) and ophthalmology consultation, repeat blood cultures, empiric echinocandin therapy, early source control, antifungal de-escalation, intravenous to oral (IV to PO) switch, and duration of therapy. The primary outcome of the study was total adherence to the CTB. The secondary outcomes include adherence with the individual components of the CTB, 30-day mortality, and infection-related length of stay (LOS).

Results. Forty-five patients in the pre-group and 24 patients in the CTB group with candidemia were identified. Twenty-seven patients in the pre-group and 19 patients in the CTB group met inclusion criteria. Total adherence with the CTB occurred in one patient in the pre-group and threepatients in the CTB group (4% vs. 16%, $P = 0.29$). ID was consulted in 15 patients in the pre-group and 17 patients in the CTB group (56% vs. 89%, $P = 0.02$). Source control occurred in three and 11 patients, respectively (11% vs. 58% $P < 0.01$). The bundle components of empiric echinocandin use (81% vs. 100%, $P = 0.07$), ophthalmology consultation (81% vs. 95%, $P = 0.37$), and IV to PO switch (22% vs. 32%, $P = 0.5$) also improved in the CTB group. Repeat cultures and antifungal de-escalation were similar among groups. Thirty-day mortality decreased in the CTB group by 10% (26% vs. 16%, $P = 0.48$). Median iLOS decreased from 30 days in the pre-group to 17 days in the CTB group ($P = 0.05$).

Conclusion. The CTB, with a BPA and linked order-set, improved guideline recommended management of candidemia specifically increasing the rates of ID consultation and early source control. There were quantitative improvements in mortality and iLOS.

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193. Validation of an Empiric Candidemia Treatment Algorithm

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Session: 44. Clinical Mycology

Thursday, October 5, 2017: 12:30 PM

Background. Judicious use of echinocandins may limit the development of resistance in *Candida* species. Guidelines endorse the use of echinocandins as initial therapy in candidemia, with fluconazole as an alternate choice in select patients. We compared the ability of providers to predict the need for echinocandin therapy in *Candida* bloodstream infections to that of a proposed institutional treatment algorithm designed to optimize empiric antifungal use.

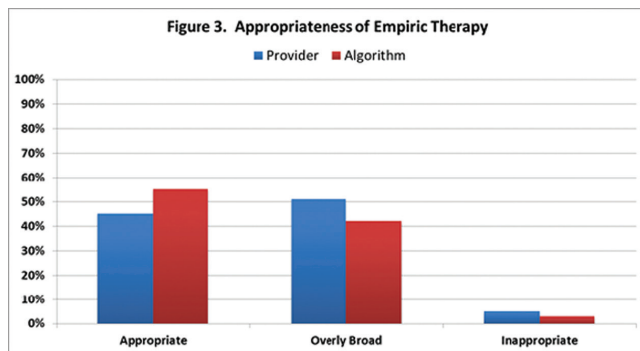
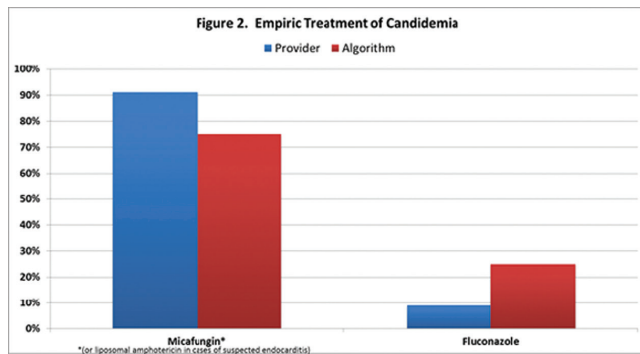
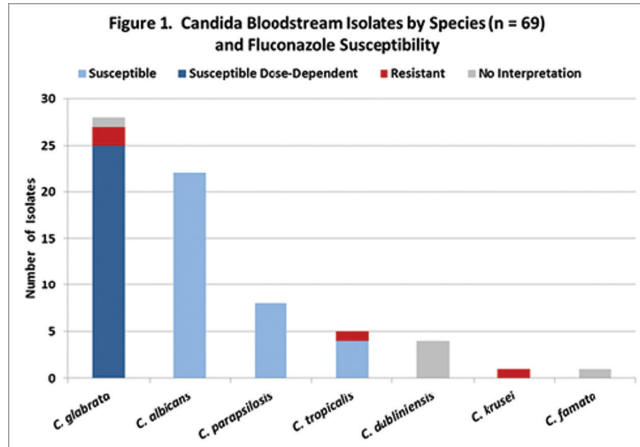
Methods. In this retrospective study (10/2015–10/2016), patients were included with *Candida* isolated in ≥ 1 blood culture, without candidemia in the prior 14 days. Empiric treatment (the first antifungal prescribed for ≥ 24 hours after index blood culture draw) was considered "overly broad" if an echinocandin was administered to a fluconazole-susceptible isolate and "inappropriate" if fluconazole was administered to a fluconazole-non-susceptible isolate. An institutional algorithm was created recommending empiric echinocandin use based on the presence of ≥ 1 risk factors (Table 1). Provider choice and the recommended agent according to the algorithm were compared with the final fluconazole susceptibility of the organism.

Results. Among 65 episodes of candidemia, the majority of isolates were *C. glabrata* (Figure 1). Ninety-one percent of patients received non-azole therapy, primarily micafungin. Fluconazole was recommended by the algorithm in 25% of cases but initially prescribed in only 9% (Figure 2). Providers prescribed both overly broad and inappropriate treatment at a higher rate than algorithm recommendations (Figure 3).

Conclusion. An algorithm using risk factors for fluconazole-non-susceptible *Candida* was able to predict appropriate empiric antifungal therapy better than provider decision making in cases of candidemia. Implementation of this algorithm into local treatment guidelines may improve empiric antifungal prescribing.

Table 1. Characteristics of candidemia episodes

Patient characteristics	Frequency	(%)
Age: mean (SD)	59.8	(17.5)
Male	27	(42)
Algorithm risk factors		
Critical illness	38	(58)
Immunosuppression	16	(25)
Intravenous drug use	16	(25)
Recent triazole exposure	11	(17)
Recent <i>C. krusei</i> or <i>glabrata</i>	4	(6)
Complicated bloodstream infection	8	(12)
≥1 algorithm risk factor	49	(71)



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194. Clinical Experience with Telavancin for the Treatment of Patients with Bone and Joint Infections: Preliminary Results from the Telavancin Observational Use Registry (TOUR™)

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Session: 45. Clinical: Bone and Joint Infection
Thursday, October 5, 2017: 12:30 PM

Background. Telavancin (TLV) is a lipoglycopeptide antibacterial active against a wide range of Gram-positive pathogens, including methicillin-sensitive and -resistant *Staphylococcus aureus* (MSSA and MRSA). Bone and joint infections represent a complex set of diseases requiring prolonged antimicrobial therapy and are commonly caused by Gram-positive pathogens, including *S. aureus*.

Methods. The Telavancin Observational Use Registry (TOUR™) is a multicenter chart review study designed to characterize infection types, pathogens, and outcomes of patients treated with TLV in clinical practice. Data from TOUR were used to characterize a subset of bone and joint patients. Clinical data including patient demographics, pathogens, outcomes, and adverse events (AEs) were analyzed. Clinical outcomes were determined by investigators' assessment.

Results. As of March 31, 2017, data for more than 1000 patients were collected from 46 sites. Of these, 286 patients were treated for bone and joint infections. Among these 286 patients, median age was 57 years (range 18–92 years) and 27% (n = 76) were aged ≥65 years, 66% (n = 189) were male, and 84% (n = 241) were White. The median body mass index was 30.0 kg/m² (range 19.2–62.7 kg/m²). MRSA was the most commonly isolated pathogen at baseline (38%; n = 108). The median TLV daily dose and duration of treatment were 750 mg (range 300–1500 mg) or 8.3 mg/kg (range 3.7–16.9 mg/kg) and 26.5 days (range 1–119 days), respectively. Telavancin was used as second-line therapy in 71% (n = 202) of patients, and the majority of patients (66%; n = 189) were treated as outpatients. Overall, 71% (n = 203) of patients were cured or improved to step-down therapy, 9% (n = 25) failed treatment, 10% (n = 30) had an indeterminate clinical outcome at end of therapy (EOT), and 10% (n = 28) had missing or undocumented outcomes. Among the patients who had outcome assessment (n = 258) at EOT, 79% were cured or improved to step-down therapy and 10% failed therapy. AEs were reported in 45 patients; six reported a serious AE, and 32 had AEs leading to TLV discontinuation.

Conclusion. In a real-world setting, once-daily TLV produced a positive clinical response in >70% of patients with difficult-to-treat bone and joint infections and may represent an alternative treatment option.

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195. Low Rate of Microbiologic Relapse in Two-Stage Exchange for Hip Prosthetic Joint Infections

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Session: 45. Clinical: Bone and Joint Infection
Thursday, October 5, 2017: 12:30 PM

Background. Prosthetic joint infection (PJI) is a grave complication of total hip arthroplasty (THA). Historically, two-stage arthroplasty exchange has been considered to be the definitive approach to eradicating infection and preserving joint function. However, patients are increasingly presenting with higher rates of comorbidities traditionally associated with poorer orthopedic surgical outcome, including advanced age, obesity and diabetes. We investigated whether two-stage exchange remains effective for THR PJI at an orthopedic specialty hospital, and what were the microbiologic etiologies in repeat infections.

Methods. A retrospective cohort of THA PJI treated with two-stage exchange was identified by query of hospital coding records from 2009 to 2014. The primary endpoint was defined as 2-year implant retention without further surgery. Failure was defined as a recurrence within 2 years. Microbiologic failure was defined as a recurrence of the previously treated organism. Descriptive statistics were completed using the Fisher's exact test for categorical variables and the Mann-Whitney U-test for continuous variables.

Results. One hundred and forty-four patients meeting Musculoskeletal Infection Society International Consensus criteria for THA PJI were identified. The average age was 65 years and 60% were female. One hundred and twenty-seven (88.2%) were cured at 2 years. Pathogens included *Staphylococcus aureus* (MSSA, 23%; MRSA, 13%), coagulase-negative staphylococci (17%), and streptococci (17%). In univariate analysis, no links were noted between primary outcome and patient age, comorbidities (including diabetes and tobacco), BMI, microbiology, or symptom duration. Of the 17 patients who did not meet criteria for success, 11 (65%) were diagnosed with new, microbiologically distinct infection. The remaining six met our criteria for microbiologic failure; four of the six patients had *S. aureus* infection (three MSSA).

Conclusion. We present 2-year outcomes on a large cohort of THA PJI treated with two-stage exchange arthroplasty. Nearly, two-thirds of the patients who failed were found to have a new infection at the time of relapse. Only 4% of the patients in our cohort failed to achieve cure of the primary infection. Two-stage exchange continues to be an effective approach to PJI treatment with a low rate of microbiologic failure.

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