1779. Prevalence of and Factors Associated with Cladhitodium difco-cide Infection Among Patients with Candidemia, United States, 2014–2016

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Session: 216. The Fungus Among us – Clinical Advances
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Background. Candidemia and Cladhitodium difco-cide infection (CDI) are two common healthcare-associated infections (HAIs) and share risk factors such as antibiotic use and prolonged hospitalization. CDI and candidemia disrupt gut microbial diversity, allowing Candida overgrowth and translocation to the bloodstream. We describe CDI co-infection among patients with candidemia.

Methods. Population-based surveillance for candidemia was conducted for CDC's Emerging Infections Program during 2014–2016. A case of candidemia was defined as a blood culture positive for Candida species collected from a surveillance area resident. Demographic and medical information, including occurrence of CDI, was collected. We defined co-infection as CDI within 90 days of candidemia and performed bivariate analysis to assess factors associated with co-infection.

Results. Among 2129 cases of candidemia, 190 (9%) had CDI co-infection; 116 (5%) had CDI in the 90 days before candidemia (median 10 days) and 66 (3%) had CDI following candidemia (median 8 days). The median age of those with CDI-candidemia co-infection was 61 years and 100 (53%) were male. Compared with candidemia alone, the odds of CDI co-infection was 2.8-fold greater for female patients (OR 2.8, 95% CI 2.0–4.0), 4.5-fold greater for patients of black race (OR 4.5, 95% CI 1.05–19.0), those with diabetes (OR 1.68, 95% CI 1.24–2.27), pancreatitis (OR 1.91, 95% CI 1.01–3.61), or solid organ transplant (OR 4.15, 9.09–8.22). Those with co-infection had higher odds of certain healthcare exposures: hemodialysis (OR 2.27, 1.57–3.28), hospital stay in the past 90 days (OR 1.9, 1.37–2.64), ICU admission in the past 14 days (OR 1.78, 1.20–2.66), and central venous catheter (CVC) at the time of candidemia (OR 1.71, 1.19–2.46). There were no significant differences in 30-day mortality or in type of Candida species, although C. parapsilosis was less common in the co-infection group (8% vs. 13%).

Conclusion. Nearly one in ten patients with candidemia also had CDI co-infection. Black race, certain underlying conditions, hemodialysis, previous hospitalization, ICU stay, and the presence of a CVC were associated with co-infection. Clinicians should be vigilant for co-infection of CDI and candidemia, particularly in situations with associated risk factors.

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1780. Routine Cryptococcal Antigen Screening in Solid Organ Transplant Recipients: Is it Time to Save Lives and Money?

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Background. Cryptococcosis affects 1 in 270 solid organ transplant (SOT) recipients with high mortality. In high-risk infected patients, cryptococcal antigen (CRAG) is detectable in blood weeks to months before symptomatic infection and screening is recommended. No screening guidelines exist for SOT recipients.

Methods. We performed a cost-effectiveness analysis of CRAG screening amongst SOT recipients. We estimated costs of screening from Medicare reimbursement of $16.49 for CPT 87899 (Infectious agent antigen detection by immunoassay). We determined the number at risk from a large cohort of 42,634 adult SOT recipients from ICD-9 CM billing data from HCUP State Inpatient Databases of Florida (2006–2012), New York (2006–2011), and California (2004–2010). Cost of screening was compared with the cost of inpatient hospitalization.

Results. Among 42,634 adult SOT recipients, 158 (0.37%) developed cryptococcosis at a median time of 15.5 months (range 0.1–80) after transplant. During the 43 month follow-up, there was approximately 2.5% annual mortality. The estimated costs for CRAG screening detected 75% of asymptomatic cryptococcal antigenemia prior to symptomatic disease requiring prolonged hospitalization, it would be approximately cost neutral ($11.5 million), and even cost saving if above 80% of hospitalizations are averted. Alternatively stated, for every one hospitalization avoided, 4245 infections were averted. Assuming the ability of routine screening to identify 75% of patients who would develop invasive cryptococcosis; CRAG screening every 3 months among SOT recipients likely would be at least cost neutral to the healthcare system. Antecedent duration of cryptococcal antigenemia prior to symptomatic disease in Non-HIV/SOT cohorts should validate this approach to save lives in a cost-effective manner.

Conclusion. Assuming the ability of routine screening to identify 75% of patients who would develop invasive cryptococcosis; CRAG screening every 3 months among SOT recipients likely would be at least cost neutral to the healthcare system. Antecedent duration of cryptococcal antigenemia prior to symptomatic disease in Non-HIV/SOT cohorts should validate this approach to save lives in a cost-effective manner.

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1781. Galidesivir, a Direct-Acting Antiviral Drug, Abrogates Viremia in Rhesus Macaques Challenged with Zika Virus

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Background. Zika virus (ZIKV) was first isolated from a sentinel rhesus monkey in 1947. ZIKV infection in humans is associated with serious neurological and reproductive complications. No antiviral or protective vaccine is yet available. Galidesivir an adenosine analog is a potent viral RNA-dependent RNA polymerase inhibitor with demonstrated broad-spectrum antiviral activity.

Methods. We have conducted four pre-clinical studies in rhesus macaques to assess antiviral efficacy and dose responses of galidesivir against ZIKV infection. Collectively, we have evaluated 70 rhesus macaques by directly infecting rhesus macaques using 1×10⁶ TCID₅₀ of a Puerto Rican ZIKV isolate. We have evaluated galidesivir therapy administered via IM injection as early as 90 minutes and up to 72 hours after subcutaneous (SC) ZIKV challenge, and as late as 5 days after intravaginal (IVAG) challenge. In these studies, we evaluated the efficacy of a range of loading and maintenance doses of galidesivir. The highest dose evaluated has been a loading dose of 100mg/kg BID followed by a maintenance dose of 25mg/kg BID for nine days. We followed multiple endpoints, including ZIKV RNA levels in plasma, urine, saliva, and cerebrospinal fluid. Immune activation, complete blood counts, chemistries and galidesivir pharmacokinetics were also monitored.

Results. Galidesivir was well-tolerated in all studies. All untreated controls developed high-level plasma viremia, and had readily detectable ZIKV RNA in CSF, saliva and urine. Animals treated in the first 24 hours after SC ZIKV challenge did not develop plasma viremia and were either negative or had significantly reduced ZIKV RNA in bodily fluids. Animals treated with galidesivir later (up to 72 hours) were partially protected; they had detectable plasma ZIKV RNA, but the onset was delayed and the magnitude significantly reduced compared with controls. Animals infected IVAG were protected by galidesivir treatment up until day 5 after infection, with no blood viremia and significant reductions in ZIKV RNA in the CSF as compared with controls.

Conclusion. Galidesivir dosing in rhesus macaques was well-tolerated and offered significant protection against ZIKV infection. These results warrant continued study and clinical evaluation.

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1782. Outcomes of women with laboratory evidence of Zika infection in pregnancy

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Session: 217. Zika - A to Z
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Background. Zika (ZIKV) infection in pregnancy is a global health concern. With onset of local transmission, obstetricians in Miami-Dade County, FL, Oral Abstracts • OFID 2017:4 (Suppl 1) • S55
United States, are now in the unique position of providing care to both pregnant women with locally-transmitted and travel-associated ZIKV infections. This study provides data regarding the testing and pregnancy outcomes of women with laboratory evidence of ZIKV infection in pregnancy.

**Methods.** A retrospective chart review was conducted using laboratory records of ZIKV testing (PCR and IgM) completed from January through December 2016 at multiple tertiary care centers located in Miami-Dade County. Testing was based on CDC guidelines at time of testing, leading to heterogeneity in tests performed. Data was extracted from charts of women with positive ZIKV PCR in serum and/or urine or positive ZIKV IgM with confirmatory, pending, or insufficient PRNT results. Routine obstetrics parameters and the presence of fetal or neonatal abnormalities were recorded.

**Results.** Of the 2327 pregnant women screened for ZIKV, 88 (3.8%) screened positive with PCR and/or IgM in serum or urine. Of those women with positive ZIKV test, 53 (68%) had no documented ZIKV symptoms and 48 (65%) had no known travel history outside of Miami-Dade County during their pregnancy. Sixty-six women had antenatal ultrasounds, 14 (21%) of which ever had a head circumference or biparietal diameter measurement less than the third percentile, but none showed evidence of intracranial calcifications. Fifty-four women with positive testing have delivered: 46 at term and 8 preterm. Fifty-four infants have been born to women with positive ZIKV testing; 2 infants (1.98%) had documented congenital abnormalities. One infant was born with clinically-defined microcephaly (1.9%) and intracranial calcifications and the other had only intracranial calcifications. Ninety-four positive IgM tests were sent to the CDC for confirmatory plaque reduction neutralization testing (PRNT). 49 PRNT tests returned positive (ZIKV titer ≥10), while 28 returned negative (ZIKV titer <10), representing a false-positive rate of 30.4%.

**Conclusion.** As this epidemic persists, data from this unique cohort of women with both local and travel-associated ZIKV exposure contributes to the growing knowledge base regarding implications of ZIKV in pregnancy.

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1783. Environmental and Climatic Risk Factors for Zika and Chikungunya Virus Infections in Rio de Janeiro, Brazil, 2015–2016

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**Session:** 217: Zika - A to Z

**Background.** From March 2015 to May 2016, 3,916 participants from 58 municipalities in the state of Rio de Janeiro were screened for ZIKV and CHKV Infections in Rio de Janeiro, Brazil, 2015–2016. Routine laboratory testing (PCR and/or IgM) demonstrated a wide range of neuronal and non-neuronal tropism. However, infection rate was highest in Tbr2+ - Intermediate Progenitor Cells (IPC; 81.4 ± 12%) and DCX+ Immature Neurons (IN; 51.5 ± 13.9%), followed by SOX2+ Nestin+ Neural Precursor Cells (NPC; 26.6 ± 13.4%). NeuN+ Mature Neurons had the lowest frequency of infection (MN; 10.0 ± 7.0 %) (Figure). Apoptosis was observed in both infected and uninfected bystander cortical neurons. A high infection frequency was also observed in non-neuronal cells (astrocytes, microglia, macrophages, lymphocytes).

**Methods.** To characterize the mechanism of ZIKV-induced human brain injury, we performed immunolabeling on brain tissue from a 20-week fetus with intrauterine ZIKV infection. Formalin-fixed sections of brain tissue were co-immunostained with ZIKV envelope antibody, as well as neuronal and non-neuronal lineage cell markers to assess infection within populations. Apoptosis was assessed by quantifying activated caspase 3-positive staining cells. Minimum 3–5 random microscopic fields per brain region were photographed and quantified in an automated fashion using the ImageJ Cell Counter plug-in. GraphPad Prism and Microsoft Excel software were used for data analysis.

**Results.** ZIKV demonstrated a wide range of neuronal and non-neuronal tropism. However, infection rate was highest in Tbr2+ - Intermediate Progenitor Cells (IPC; 81.4 ± 12%) and DCX+ Immature Neurons (IN; 51.5 ± 13.9%), followed by SOX2+ Nestin+ Neural Precursor Cells (NPC; 26.6 ± 13.4%). NeuN+ Mature Neurons had the lowest frequency of infection (MN; 10.0 ± 7.0 %) (Figure). Apoptosis was observed in both infected and uninfected bystander cortical neurons. A high infection frequency was also observed in non-neuronal cells (astrocytes, microglia, macrophages, lymphocytes).

**Conclusion.** Our study provides valuable insights into ZIKV pathogenesis in the fetus; it is the first to demonstrate differential infectivity/susceptibility of neuronal lineage cells to ZIKV, and evidence of apoptosis in and around these cells. The high frequency of ZIKV+ IPC and IN implies that that infection can be supported until the immature stage of neuronal differentiation. The resistance of mature neurons to ZIKV infection may also explain why ZIKV infection in the third trimester poses less risk of microcephaly in infants. The high infection rate of non-neuronal cells also suggests potential contribution of immune-mediated mechanisms of brain injury in the setting of congenital ZIKV infection.

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