2365. Volatile Metabolite-Based Detection of Clostridium difficile Infection (CDI)
Obadah Aloum, MBCChB1; Mahesh I. Thalavitiya Acharige, PhD2; Nour Ismail, MD2; Mohamad Hejazi, MD2; Yibai Zhao, PhD2; Rai Bahalabrahmanian, ScD3; Sophia Koo, MD, SM4; 1Harvard Medical School, Brigham and Women’s Hospital, Boston, Massachusetts; 2North Florida Regional Medical Center, University of Central Florida, Gainesville, Florida; 3University of Massachusetts Amherst, Issaquah, Washington; 4Brigham and Women’s Hospital, Dana-Farber Cancer Institute, Boston, Massachusetts

Background. CDI is a frequent cause of morbidity and mortality in hospitalized patients. Despite advances in rapid CDI testing, there are often delays between the onset of symptoms and receipt of test results. We sought to test the hypothesis that the altered CDI intestinal microbiome has a unique volatile metabolite profile, distinct from the profile of patients with other causes of antibiotic-associated diarrhea, which potentially can be used to identify patients with CDI.

Methods. We prospectively collected fresh stool samples from inpatients with suspected CDI at an academic tertiary care hospital from July 2015 to November 2017, adsorbed volatile metabolites from each sample onto sorbent tubes within an hour of sample collection, and used thermal desorption-gas chromatography/tandem mass spectrometry to identify each metabolite. All patients were exposed to at least one antibiotic agent in the prior 90 days, and only patients receiving empiric CDI treatment or with formed stool samples were excluded. We used logistic regression models, adjusting for prior anti-anaerobic antibiotic therapy and CDI severity (serum albumin <3 g/dL and WBC ≥ 15,000/mm³ or abdominal tenderness) and adjusting for multiple testing using Storey’s q-value procedure (with a threshold of q ≤ 0.05), to examine the relationship between CDI, as determined by the reference standard of the cell culture cytotoxicity neutralization assay, and each metabolite.

Results. In our 565-patient cohort, median age was 61 years (IQR 50, 70) and 277 (49%) were male; 173 (31%) had abdominal pain in the 24 hours before testing, 59 (10%) had fevers in the prior 24 hours, 22 (4%) had an ileus, 74 (13%) had mental status changes in the prior 24 hours, 89 (16%) were hospitalized in the ICU at the time of testing, 45 (7%) had receiving pressors, 82 (15%) had a WBC ≥ 15,000/mm³, and 137 (24%) had a serum lactate > 1.5 mmol/L. Ultimately, 155 patients were diagnosed with CDI. Ten metabolites (Table 1, Figure 1) were differentially distributed in patients with and without CDI.

Conclusion. We identified a suite of volatile metabolites that differentiates stool from patients with and without CDI; this profile may ultimately be used to identify patients with CDI.

Table 1. Significantly increased volatile metabolite in patients with CDI.

| Volatile Metabolites | q-value |
|----------------------|---------|
| 3-methylhexan         | <0.01   |
| Methanethiol          |         |
| N,N-dimethylmethanilene | 0.03 |
| 2,4-dialyl-1-butanol  |         |
| Ethyl Acetate         | 0.03    |
| Acetophenone          |         |
| 1,2-dithiolblibenzenene | 0.03 |
| 1-propanol            |         |
| 1,2-ethanediol         |         |

Disclosures. All authors: No reported disclosures.
before and after implementation of a two-step algorithm for the diagnosis of CDI. The pre-implementation period was defined between May 8, 2016 and May 7, 2017, and the post-implementation period was May 8, 2017 to May 7, 2018. Patients were excluded if they were admitted to a pediatric ward, tested for CDI at an outside facility, or if results were available following discharge. The primary outcome was inpatient days of metronidazole and non-parenteral vancomycin per PCR positive patient. Secondary outcomes included defined daily doses of therapy, proportion of untreated patients, time to resolution of diarrhea, all-cause in-hospital mortality, 30-day recurrence, all-cause 30-day readmission, length of stay, and 30-day CDI-related complications. CDI-related complication was a composite of ICU care, megacolon, ileus, surgical intervention. It was calculated that 242 patients were required to achieve at least 80% power to detect a 30% difference in antibiotic days between pre- and post-implementation of two-step C. difficile testing. Wilcoxon two-sample test was used for continuous data, and χ² or Fisher exact test were used for categorical data.

Results. The results suggests that toxin EIA may help differentiate between colonization and active infection.

Conclusion. Incorporation of C. difficile toxin EIA to PCR for the diagnosis of CDI resulted in a significant reduction in non-parenteral vancomycin and metronidazole days of therapy. Patient outcomes were not adversely affected by the addition of toxin EIA. The results suggests that toxin EIA may help differentiate between C. difficile colonization and active infection.

Disclosures. All authors: No reported disclosures.

2367. Selecting Testing Frequency for Estimation of Incubation Periods: A Simulation Study Based on Clostridioides difficile Observations
Brigid Wilson, PhD; Mustafa S. Ascha, MS, PhD; Justin O’Hagan, ScD; Curtis Donksky, MD; Louis Stokes Cleveland VA Medical Center, Cleveland, Ohio; Case Western Reserve University, Cleveland, Ohio; Centers for Disease Control and Prevention, Atlanta, Georgia; Cleveland VA Medical Center, Cleveland, Ohio

Session: 250. HAI: C. difficile - Diagnostic Testing
Saturday, October 5, 2019: 12:15 PM

Background. Estimates of the incubation period (time between pathogen transmission and symptom onset) for an infection inform infection control and prevention measures. However, observation of the exact transmission and onset times rarely occurs and “coarse,” or doubly interval-censored, data about these exact times are typically used for estimation. The effect of coarseness on the required number of symptomatic cases and the uncertainty of the estimates is unknown, prompting a simulation study informed by data from an investigation of the incubation period of Clostridioides difficile.

Methods. We simulated incubation period data assuming a log-normal distribution, a true median incubation period of 7 days, and a standard deviation of 1 day for sample sizes of 50 to 300 symptomatic cases. For each sample size, we simulated 1000 datasets and examined the impact of testing frequencies, considering intervals between tests of 0.25 to 2 times the median incubation period (1.75 to 14 days) about both transmission and symptom onset times. With these doubly interval-censored observed values, we fit accelerated failure time models to estimate the median incubation time and its 95% confidence interval (CI). Comparing the coverage of the true median and the widths of the CIs, we summarized simulation results across sample sizes and testing frequencies.

Results. Model results from all combinations of sample sizes and testing frequencies yielded median incubation period CIs close to the target 95% coverage level (Figure 1). The width of the 95% CI about the median decreased with larger sample sizes and shorter times between tests (Figure 2). Thus, similar estimates and confidence intervals would be observed from 100 symptomatic cases with a testing frequency of 3.5 days as from 200 symptomatic cases tested every 14 days.

Conclusion. The frequency of testing is a key factor in planning studies to estimate incubation periods for infectious diseases. To achieve a desired degree of certainty in estimation, increased frequency of testing can reduce the number of symptomatic cases required. We showed that simulations can assist in planning natural history studies, and these methods could be extended to include population data (e.g., transmission incidence) and cost constraints.

Disclosures. All authors: No reported disclosures.

2368. Molecular Epidemiology of Clostridioides difficile Infections in Pediatric Oncology and Transplant Patients
Ruba Barbar, MD; Hana Hakim, MD, MS, CIC; Randall Hayden, MD; Randall Hayden, MD; Cherylyn D. Garner, PhD, D(ABMM); Jessica B. Brazelton de Cardenas, PhD; Karen C. Carroll, MD; Dimitrios Bourdas, MLS(ASCP)CM; Shavana Kimberly Carroll, BA; St. Jude Children’s Research Hospital, Memphis, Tennessee; St Jude Children’s Research Hospital, Memphis, Tennessee; Johns Hopkins Hospital Microbiology, Baltimore, Maryland; Johns Hopkins Hospital, Baltimore, Maryland; Hopkins Hopkins University,

Disclosures. All authors: No reported disclosures.