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**470. Concomitant Antibiotic Use and Death Among a National Cohort of Veterans With Clostridium difficile Infection (CDI)**

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and after CDI events. The CDPH HAI Program is using these analyses to inform CDI prevention outreach to California healthcare facilities and provider networks.

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#### 467. Investigation of a *Clostridium difficile* Infection (CDI) Outbreak in a Community Teaching Hospital

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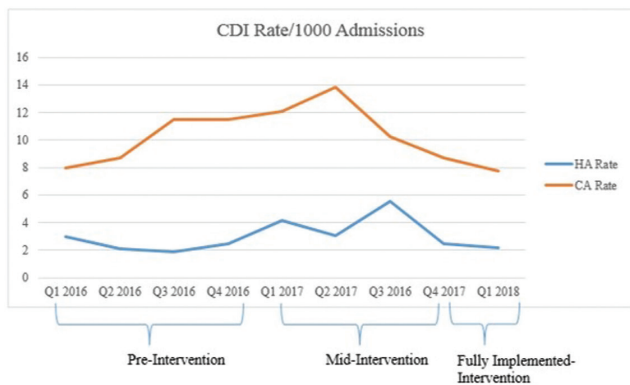
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**Background.** An abrupt change in baseline CDI from 2016 to 2017 prompted a response team task force including senior administration, the CMO, infection prevention, environmental services, laboratory, pharmacy, emergency department (ED), and nursing to address the problem.

**Methods.** Hospital-acquired (HA) and community-acquired (CA) CDI cases were tracked using an epidemic curve and institutional case mapping. A multipronged intervention was implemented that included molecular typing of isolates, quarterly terminal cleaning of the ED, improved CDI screening and testing, intensified antimicrobial stewardship (AS) with mandatory education for key clinicians, and rigorously enhanced enforcement of hand hygiene with secret observers and directed feedback. Pre-, mid-, and fully-implemented intervention HA and CA CDI rates were observed.

**Results.** Ninety-five percent of CA CDI and 98% of all patients who developed HA CDI were admitted through the ED. Cases of CDI were distributed throughout the hospital. The genotyping did not identify a single strain outbreak. Sixteen percent of all CDI samples (23% of CA and 9% of HA cases) sent to the DOH tested positive for BINAP1. Preintervention rates of HA CDI were found to be lower than mid-intervention rates (2.4, 95% CI= 1.5–3.1 vs. 4.3, 95% CI= 1.13–7.37). HA CDI rates after full-intervention in fourth quarter 2017 and first quarter 2018 trended toward baseline (2.1, 95% CI = 0–5.93) but had not achieved statistical improvement (Figure 1). A significant correlation between HA CDI rates and CA CDI rates was not found ( $r = 0.241$ ,  $P < 0.5$ ), suggesting that HA CDI rates were not driven by CA CDI rates. Hospital and ED hand hygiene improved significantly; hospital preintervention = 0.84 vs. intervention = 0.91,  $P < 0.01$ ; ED hand hygiene preintervention = 0.72 vs. intervention = 0.86,  $P < 0.04$ . No statistically significant changes in antimicrobial use were noted.

**Conclusion.** A rapid, aggressive team-based approach for a CDI outbreak successfully reversed a rising rate and SIR. Although no one specific intervention was clearly responsible for the reversal, we did observe a statistically significant increase in hand hygiene. This outbreak and its management illustrate the importance of active surveillance and a rapid team-based response to CDI outbreaks.



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#### 468. Diagnosis of Clinical *Clostridium difficile* Infection: An Unmet Challenge

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**Background.** Diagnosis of *Clostridium difficile* infection (CDI) is challenging. The reason is two-fold: (a) lack of unique symptoms and (b) lack of a gold standard test for CDI. We studied variation in CDI rates when different diagnostic algorithms were utilized. In addition, we compared patients who met the clinical definition of CDI with different diagnostic assays.

**Methods.** This is a retrospective study at an academic medical center (401-bed) conducted over 12 months (January 2017–December 2017). A stool sample that tested positive by polymerase chain reaction (PCR) for *C. difficile* ( $n = 81$ ) was then tested for glutamate dehydrogenase (GDH) and toxin enzyme immunoassay (EIA). Additionally, all PCR-positive cases were also tested for toxin production by cytotoxic neutralization assay (CCNA). Clinical *C. difficile* was defined as three or more loose stools within

24-hour time period. Clinical data were obtained from review of charts. This definition was applied to all community-onset and hospital-onset cases.

**Results.** *C. difficile* was detected in 81 symptomatic patients by PCR test. Of these, 41.9% met the clinical definition of diarrhea. Of the 81 patients, toxin EIA and GDH were positive in 29.6% (24/81) and 4% met the clinical definition. CCNA was positive in 66.67% (54/81) and only 9% met the clinical definition. The CDI rate (per 10,000 patient days) was 10.2 in the PCR positive group; 3.02 in toxin EIA and GDH group and 6.81 in CCNA group. Duration of diarrhea was longer when functional assays (toxin EIA and/or CCNA) were positive, i.e., 48 hours after diagnosis, 22.7% (18/79) of patients with a positive CCNA and EIA had diarrhea while only 6% (3/49) of the patients with GDH and PCR positive tests (nonfunctional assays) had diarrhea ( $P = 0.013$ ). The difference was statistically significant. All 81 patients were started on CDI treatment within 24 hours of diagnosis. Of note, there was no laxative use contributing to symptoms in these cases.

**Conclusion.** CDI rates differ with various diagnostic algorithms. Duration of diarrhea was significantly longer when functional assays (CCNA or toxin EIA) were positive. Inclusion of both a functional assay (EIA and/or CCNA) and a clinical definition of CDI can improve the diagnostic accuracy of CDI. A combination of clinical judgment and functional assays is required for an accurate diagnosis of CDI.

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#### 469. Validation and Characterization of Community-Acquired *Clostridium difficile* Infections from the Quebec *C. difficile* Infection Surveillance Program (QCISP)

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**Background.** Community-acquired *Clostridium difficile* infections (CA-CDI) are under a mandatory reporting program starting in August 2004 across 95 healthcare institutions from the QCISP. There has been a slow and continuous increase in the incidence rate of hospitalized CA-CDI since 2007 without any known obvious explanation. The objectives of this study were to characterize cases of CA-CDI and investigate the potential causes of this increase.

**Methods.** A retrospective study was carried out using a survey sent to eligible healthcare institutions. Hospitals participating in QCISP that reported  $\geq 3$  cases of CA-CDI in 2016–2017 were invited to participate. To identify potential causes of the apparent increase in CA-CDI incidence, they were asked to provide clinical information regarding up to three cases of CA-CDI for two distinct surveillance years (2011–2012 and 2016–2017). To characterize each CA-CDI cases, a broad range of demographic, clinical, and laboratory variables were collected, including medical history, history of contact with primary and secondary healthcare institutions, previous antibiotics use as well as laboratory diagnostic test. A  $\chi^2$  test have been used to test year differences in indicator distributions.

**Results.** A total of 49 healthcare institutions provided data on 172 cases of CA-CDI. Overall, 92% ( $n = 159$ ) of them meet the QCISP CA-CDI criteria definition. Among them, most patients (67%) were female, and average age was  $66.7 \pm 20.5$  year old. Seventy-four percent had received antibiotic in the previous year. Between the two years, there was no significant change in the socio-demographic and clinical variables of CA-CDI cases. The proportion of patients receiving immunosuppressive drugs and proton pump inhibitors at the time of diagnosis was 11% and 45%, respectively. The proportion of cases visiting ambulatory healthcare settings during the year previous to patient admission increased from 61% (2011–2012) to 69% (2016–2017) ( $P = 0.18$ ). Moreover, there was a significant increase in the proportion of CA-CDI diagnosed by laboratory PCR test (from 8% to 55%;  $P < 0.0001$ ).

**Conclusion.** This study provided important data to characterize CA-CDI using the QCISP. The increase in the use of PCR is associated with the incidence of CA-CDI but may not be the cause of it.

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#### 470. Concomitant Antibiotic Use and Death Among a National Cohort of Veterans With *Clostridium difficile* Infection (CDI)

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**Background.** Antibiotic use is a well-known risk factor for development of CDI, and there is preliminary evidence suggesting concomitant antibiotic use may result in poor outcomes, including death. This work investigated the effect of concomitant antibiotic exposure during CDI treatment on mortality among patients with CDI.

**Methods.** We conducted a national retrospective study of Veterans with a first CDI between 2010 and 2014, defined as a positive *C. difficile* toxin(s) and no episode in the year prior. Those treated with guideline recommended CDI treatment were included (10–14 days of PO or IV metronidazole, PO or PR vancomycin, or fidaxomicin). The exposure of interest was any non-CDI antibiotic use during CDI treatment; and the outcome was all cause death within 30 days of the end of CDI treatment. Inverse probability of treatment weighted Cox proportional hazards models were used to estimate the effect of concomitant antibiotic use on time to mortality. Weights were derived from propensity score modeling of the probability of exposure to antibiotics during CDI treatment as a function of potential confounders. Sensitivity analyses by antibiotic class were conducted.

**Results.** Of the 9,517 patients included in the study cohort, mean age was 65.3 years ( $\pm$ SD 14.6), 92.5% ( $n = 8,802$ ) were male, and 75.03% ( $n = 7,141$ ) were white. Half were exposed to non-CDI antibiotics during CDI treatment (51.8%,  $n = 4,925$ ) and 8.9% ( $n = 849$ ) died. In unadjusted and adjusted analyses, concomitant antibiotic use was associated with death (HR 5.74, 95% CI 4.75–6.93; aHR 2.39, 95% CI 2.07–2.75). Advanced generation cephalosporin (aHR 2.36, 95% CI 2.05–2.71),  $\beta$ -lactam/ $\beta$ -lactamase inhibitor combinations (aHR 1.45, 95% CI 1.16–1.82), and clindamycin (aHR 1.95, 95% CI 1.26–3.02) were associated with death, while fluoroquinolone use was not (aHR 0.97, 95% CI 0.84–1.12).

**Conclusion.** Among our national cohort, concomitant antibiotic use was common during CDI treatment. Any concomitant antibiotic use increased the risk of death; however, results suggest risk might vary by antibiotic class. Results support continued efforts in the reduction of unnecessary antibiotic use during CDI treatment, and future studies into which antibiotics may have the least risk of death when treatment is necessary.

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#### 471. Prevalence and Characteristics of *Clostridioides difficile* Infection in Bangladesh

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**Background.** The estimated prevalence of *Clostridioides difficile* infection (CDI) in several South Asian countries is 10.5%, similar to that in North America and Europe. However, the epidemiology of CDI in Bangladesh is unknown. We aimed to assess the prevalence of CDI and assess hospital environmental contamination of toxigenic *C. difficile* in Bangladesh.

**Methods.** This was a prospective observational cohort study at two large tertiary care centers in Dhaka, Bangladesh, conducted from January 2017 to December 2017. Stool samples were collected from hospitalized adults with diarrhea ( $\geq 3$  loose stools in a 24-hour period) and antimicrobial exposure within the past 30 days. Hospital environmental samples were collected by swabbing surfaces of common areas in the hospital. All samples underwent toxigenic culture. *C. difficile* isolates were tested for toxins A and B and PCR-ribotyped.

**Results.** Of 204 stool samples collected, 16 (7.8%) were positive for toxigenic *C. difficile*. Patients with CDI shared a room with significantly more patients (Table 1). Of 392 environmental samples, 48 (12.2%) were positive for toxigenic *C. difficile*, which was more common in patient care vs. nonpatient care areas (14.4% vs. 7.8%,  $P = 0.057$ ). Twelve clinical stool isolates and 42 environmental isolates were ribotyped. Ribotypes identified in stool isolates were F017 (50%), FP053-163 (17%), FP435 (17%), F106 (8%), and F014-020 (8%). With the exception of FP435, these were also the most common ribotypes in environmental isolates: F017 (24%), FP053-163 (12%), F106 (26%), and F014-020 (10%).

**Conclusion.** For the first time, we report the prevalence of CDI and ribotypes in at risk patients in Bangladesh. Rates and ribotypes are similar to other resource-rich or resource-limited countries.

**Table 1:** Demographic Data for All Stool Samples

Variable	No toxigenic <i>C. difficile</i> ( $n = 188$ )	Toxigenic <i>C. difficile</i> ( $n = 16$ )	<i>P</i>
Female sex, $n$ (%)	77 (41)	9 (56)	0.234
Age, years, median (IQR)	46 (32–58)	39 (25–53)	0.212
Hospital A, $n$ (%)	149 (79)	13 (81)	>0.99
Length of prior hospital stay, days, median (IQR)	13 (7–23)	14 (8–32)	0.798
Duration of previous antibiotics, days, median (IQR)	10 (7–17)	12 (6–20)	0.687
Number of patients in the same room, median (IQR)	13 (7–19)	19 (14–20)	0.009

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#### 472. Prevalence, Risk Factors, and Outcome of Postoperative *Clostridium difficile* Infection After Orthopedic Surgery

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**Background.** The patients undergoing orthopedic surgery may have many risk factors of *Clostridium difficile* infection (CDI), including increased age, multiple underlying comorbidities, the use of perioperative antibiotics, and prolonged length of stay. The aim of this study was to identify prevalence, risk factor, and outcome of postoperative CDI in patients who underwent orthopedic surgery.

**Methods.** We performed a retrospective cohort study including all patients aged  $\geq 18$  years who underwent orthopedic surgery from January 2016 through December 2017 in a tertiary care hospital in Seoul, South Korea.

**Results.** During the study period, 7,369 episodes of orthopedic surgery were identified. The prevalence of *C. difficile* infection was 7.7 cases per 1,000 surgical procedures (95% confidence interval, 6.0–10.0). The risk of CDI was the highest among patients who underwent spine surgery (33.8 cases per 1,000 surgical procedures), followed by hip/femur surgery (12.4), knee (3.8), and extremity (3.2). The risk of CDI increased according to the increase in duration of proton pump inhibitor: 0.1% (no use), 0.3% (1–7 days), and 2.7% (>7 days,  $P < 0.001$ ). The independent risk factors associated with postoperative CDI were age (odds ratio [OR] per 1-year increase, 1.04;  $P < 0.001$ ), Charlson comorbidity index score (OR per 1-point increase, 1.26;  $P < 0.001$ ), duration of proton pump inhibitor (OR per 1-day increase, 1.02;  $P < 0.001$ ), and operation time (OR per 1-hour increase, 1.30;  $P = 0.003$ ). Of 6,724 episodes of surgical procedure for which patients received exclusively perioperative antibacterial prophylaxis, 22 episodes of postoperative CDI occurred (3.2 cases per 1,000 surgical procedures). Among this subgroup, the risk of CDI increased according to increase in duration of antibacterial prophylaxis: 0% (<24 hour), 0.28% (1–7 days), and 1.27 (>7 days;  $P < 0.001$ ). After adjusting confounding factors, duration of perioperative antibacterial prophylaxis remained a significant risk factor for postoperative CDI (OR per 1-day increase, 1.11;  $P < 0.001$ ). Patients with CDI had a higher rate of postoperative mortality (10.5% vs. 0.6%;  $P < 0.001$ ) and an increased length of hospital stay (mean 42 vs. 10 days;  $P < 0.001$ ).

**Conclusion.** Judicious use of proton pump inhibitor and avoiding of extension of prophylactic antibiotics can reduce postoperative CDI after orthopedic surgery.

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#### 473. Molecular Typing of *Clostridium difficile*: Concordance Between PCR-Ribotyping and Multilocus Sequence Typing (MLST)

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**Background.** *Clostridium difficile* infection (CDI) incidence has increased dramatically in the past decade, making CDI one of the most common causes of infectious diarrhea and an urgent public health threat. Understanding the biological features and spread of *C. difficile* strains can help target control efforts. PCR-ribotyping, the current method of choice for *C. difficile* typing, remains subjective and challenging for inter-laboratory comparisons. Multilocus sequence typing (MLST), based on the alleles of seven housekeeping genes, represents a more robust tool that would enhance inter-laboratory reproducibility. However, a comprehensive translation system to ribotyping is a prerequisite. Here, we describe the concordance between MLST and PCR-ribotyping.

**Methods.** The Centers for Disease Control and Prevention's (CDC) Emerging Infections Program (EIP) conducts CDI surveillance in 10 US sites. *C. difficile* isolates cultured from a subset of cases underwent capillary-based PCR-ribotyping at CDC. A representative sample, selected from the top 30 ribotypes (RTs), underwent whole genome sequencing (WGS) at Minnesota Department of Health. An additional subset of isolates, representing the top 10 RTs, underwent WGS at CDC. At both laboratories, the Illumina MiSeq platform was used to obtain 250 bp paired-end sequencing reads. MLST analyses were done using the pubMLST *C. difficile* scheme.

**Results.** A total of 479 *C. difficile* isolates, including at least 10 isolates for each RT, were analyzed by WGS. Among the 30 RTs represented, 35 different MLST sequence types (STs) were identified. Twenty-two of the RTs (including 027) were each associated with a single unique ST, while 8 RTs (020, 014, 015, 076, 046, 153–251, A27, and 075) presented more genetic diversity with single-locus or double-locus variants, resulting in multiple STs within one ribotype. There were two instances of two different RTs sharing the same ST.

**Conclusion.** Multilocus sequence typing and PCR-Ribotyping showed comparable discriminatory abilities. However, the ST is not always predictive of the RT and vice versa. This represents the first step toward a transition to using WGS for standard *C. difficile* typing.

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