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Investigation of a cluster of *Clostridium difficile* infections in a pediatric oncology setting

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Abstract

Background: We investigated an increase in *Clostridium difficile* infection (CDI) among pediatric oncology patients.

Methods: CDI cases were defined as first *C difficile* positive stool tests between December 1, 2010, and September 6, 2012, in pediatric oncology patients receiving inpatient or outpatient care at a single hospital. A case-control study was performed to identify CDI risk factors, infection prevention and antimicrobial prescribing practices were assessed, and environmental sampling was conducted. Available isolates were strain-typed by pulsed-field gel electrophoresis.

Results: An increase in hospital-onset CDI cases was observed from June-August 2012. Independent risk factors for CDI included hospitalization in the bone marrow transplant ward and exposure to computerized tomography scanning or cefepime in the prior 12 weeks. Cefepime use increased beginning in late 2011, reflecting a practice change for patients with neutropenic fever. There were 13 distinct strain types among 22 available isolates. Hospital-onset CDI rates decreased to near-baseline levels with enhanced infection prevention measures, including environmental cleaning and prolonged contact isolation.

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SUPPLEMENTARY DATA

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.ajic.2015.09.004.

Conflicts of interest: None to report.

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Conclusion: *C difficile* strain diversity associated with a cluster of CDI among pediatric oncology patients suggests a need for greater understanding of modes and sources of transmission and strategies to reduce patient susceptibility to CDI. Further research is needed on the risk of CDI with cefepime and its use as primary empirical treatment for neutropenic fever.

Keywords

Epidemiology; Hematology; Oncology; *Clostridium difficile*

Clostridium difficile is an anaerobic, spore-forming bacillus whose presentation in children ranges from asymptomatic colonization to severe colitis and death.[1] Host factors, including cancers, can predispose to *C difficile* infection (CDI).[2,3] Among U.S. children hospitalized with cancer, CDI incidence between 1999 and 2010 increased from 7.3–13.4 infections per 10,000 inpatient days.[4]

In June 2012, an increase in CDI was noted in a children's hospital among patients in the Center for Cancer and Blood Disorders (CCBD) program (hematology, oncology, and bone marrow transplant [BMT]). Public health officials were notified, and enhanced infection prevention measures were implemented (Table 1). However, by August 2012, CDI rates remained persistently elevated, and a formal investigation by the Colorado Department of Public Health and Environment and Centers for Disease Control and Prevention (CDC) was requested.

The primary objectives of this investigation were to determine the nature and extent of CDI in CCBD patients, evaluate risk factors for CDI in CCBD patients, determine potential modes of transmission, and implement interventions to stop transmission.

METHODS

Case finding

Results of inpatient and outpatient *C difficile* stool tests performed during routine clinical care from December 1, 2010-September 6, 2012, were reviewed. The hospital switched from stool toxin enzyme immunoassay testing to polymerase chain reaction (PCR) testing (Xpert; Cepheid, Sunnyvale, CA) on December 1, 2010.

Case definitions

First incident cases were defined as first *C difficile* positive stool tests (CDPSTs) collected between December 1, 2010, and September 6, 2012, from a CCBD patient.

Duplicate cases were defined as CDPSTs collected ≤ 14 days after a prior CDPST.

Recurrent cases were defined as CDPSTs collected >14 to ≤56 days after a prior CDPST.

Subsequent incident cases were defined as CDPSTs collected >56 days after a prior CDPST that were not duplicates.

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Incident cases were further classified as hospital onset (HO) if stool was collected on or after hospital day 4 (day of admission being hospital day 1) and as community onset (CO) if stool was collected as an outpatient or prior to hospital day 4, consistent with CDC definitions.[5]

CO cases were further classified as either hospital associated if case patients had an overnight hospital stay ≤4 weeks before the CDPST, ambulatory care associated if the case patient had any outpatient visit ≤ 4 weeks before the CDPST, or both.

Cases considered to represent asymptomatic colonization were excluded if medical records documented formed stools on the test date. The laboratory rejected formed stools per policy unless overridden by a physician.

Case description

A detailed review of medical records and parent-caregiver interviews were conducted for case patients with first incident CDI occurring between June 1 and September 6, 2012. Medical records were reviewed for the 12 weeks before the case patient's first CDPST. All data were collected using standardized abstraction forms, including patient demographics, comorbidities, hospital locations, invasive devices, procedures, medications, diarrheal symptoms, outcomes of infection, and patient disposition. Parents-caregivers or patients (if ≥18 years old) were interviewed using standardized questionnaires to collect additional exposure data from the 12 weeks before the first CDPST.

Case-control study

Case patients with first incident CDI occurring between June 1 and September 6, 2012, were included in a case-control study to evaluate risk factors. Approximately 3 CCBD controls per case were randomly selected and not matched to individual cases. Because nearly all cases had an inpatient admission in the 12 weeks before diagnosis, controls were required to have a history of an overnight hospital stay from May 1-September 6, 2012. Because cases were distributed throughout June-August 2012, a random incident date was selected from June 1-September 6, 2012, for each control for data abstraction purposes. Eligible controls were excluded if new diarrhea (≥3 loose or liquid stools/24 hours) was documented in the medical record ≤3 days before the incident date.

Statistical analysis

Cases and controls were compared using logistic odds ratios for dichotomous or categorical variables and the Wilcoxon rank-sum test for continuous variables. Statistical significance was defined as a $P < .05$.

Variables with $P < .10$ were incorporated into a multivariable logistic regression model in a forward, step-wise fashion. Variables were retained if their P value remained <.05 or if they significantly improved the model's fit by likelihood-ratio testing ($P < .05$). Analyses were performed in Stata 11.1 (StataCorp, College Station, TX).

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Setting and infection prevention assessment

The children's hospital contained a single, dedicated floor for the CCDB outpatient clinic and the 24-bed inpatient ward. BMT inpatients occupied 4–12 beds in a closed section at the end of the ward. Each inpatient room had a dedicated bathroom. The BMT and regular inpatient areas had separate nursing staff, family rooms, kitchen, playrooms, and family bathrooms. When the inpatient ward was at capacity, additional patients were housed in an overflow ward.

Observations and staff interviews were conducted on the CCBD outpatient clinic, inpatient ward, and overflow ward. This included interviews of managers, nurses, and environmental cleaning staff; observations of staff workflow; hand hygiene and personal protective equipment use; staff and patient-family use of common areas; and environmental cleaning.

Environmental sampling

We obtained swabs of high-touch surfaces in CDI patient rooms and common areas of the CCBD inpatient ward and outpatient clinic to culture for *C difficile*. For each large surface area sample, we wiped a surface up to 1 m^2 with a sterile premoistened 3M Sponge-Stick (3M, St Paul, MN). Sponges were then placed in sterile bags, sealed, refrigerated, and transported to the CDC. The sponges were then processed by adding 90 mL of phosphate buffered saline with 0.02% tween 80 and homogenized in a stomacher at 260 rpm for 1 minute. The resulting eluent was concentrated by centrifugation, and the pellet was resuspended to a volume of approximately 3 mL. Duplicate 0.5 mL aliquots were plated on prereduced *C difficile*–selective media, taurocholate cycloserine cefoxitin fructose agar (TCCFA), and the remainder was added to cycloserine cefoxitin fructose broth. All cultures were incubated anaerobically at 35°C-37°C for 48 hours. Broths were then subcultured onto TCCFA plates.

For each small surface area sample, we sampled approximately 9 cm^2 with a sterile swab premoistened with sterile saline solution. The swab was then sealed, refrigerated, and transported to the CDC, where the swab was processed by adding 3 mL of phosphate buffered saline with 0.02% tween 80 and extracted by vortexing. Various concentrations of the resulting extract were placed on TCCFA.

For each water sample (from sinks, showerheads, water fountains, and facility water tanks), we collected 1 L of water in a sterile container with sodium thiosulfate tablets. On receipt by the CDC laboratory, 10 mL water was passed through a sterile 0.45 μmfilter and placed on a trypticase soy agar plate, and 0.1 mL of water was also spread on a TSA plate. The remaining volume was filtered and placed on a MacConkey agar plate.

Dust samples were collected using single-use sampling cassettes with 0.4 μm polycarbonate filters (Zefon International, Ocala, FL), which were attached to an air sampling pump (SKC, Eighty Four, PA). An area of approximately 100 cm^2 was sampled using the cassette's open nozzle. The polycarbonate filter was then directly cultured on TCCFA. All plates were incubated anaerobically for 24–72 hours at 37°C.

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All environmental sampling and processing were performed according to standardized protocols developed by the Clinical and Environmental Microbiology Branch of the Division of Healthcare Quality Promotion at the CDC.

Antimicrobial prescribing assessment

Using an internal drug utilization database, antimicrobial use rates were calculated for CCBD patients from December 2010-August 2012.

Isolate analysis

A convenience sample of *C difficile* isolates from the stool of case patients and other patients with prior CDI who either remained hospitalized or returned to the outpatient clinic for scheduled appointments were obtained. Stool from patients with recent CDI was collected to evaluate for persistent shedding as part of an infection prevention evaluation during the investigation.[6] Isolates were characterized at the CDC using multiplex PCR testing for the presence of toxin A, toxin B, and binary toxin; detection of toxin C deletions using capillary electrophoresis; and pulsed-field gel electrophoresis (PFGE) to determine strain type and relatedness.

RESULTS

Case finding

A total of 358 *C difficile* stool tests were performed among CCBD patients from December 1, 2010-August 29, 2012 (Fig 1). Ninety-five CCBD cases were identified and were classified as 69 first incident, 18 recurrent, and 8 subsequent incident cases (Fig 2). First incident CCBD cases increased from a baseline of 2.7 to 7 cases/mo in June 2012, an increase persisting through July and August (Fig 2). From December 2010-May 2012, the average number of monthly tests performed among CCBD patients was 15.2; of these, 26% were positive. In June 2012, 20 tests were performed; of these, 50% were positive. In July and August 2012, the number of tests performed increased (39 and 30, respectively), whereas positivity decreased to baseline (21% and 27%, respectively). There was no increase in testing or cases among non-CCBD patients throughout this period.

HO CDI cases comprised most of the increase in first incident CCBD cases between June-August 2012 (Fig 3). The CCBD HO CDI incidence rate during June-August 2012 was 51.7 per 10,000 patient days compared with a rate of 15.1 in 2011 and 15.4 in January-May 2012. The HO CDI rate for non-CCBD patients during June-August 2012 was 1.5 per 10,000 patient days and was similar to previous rates. The number of CO CDI CCBD cases varied from month to month (Fig 3), and all had either an inpatient admission or ambulatory care visit in the prior 4 weeks.

Case description

Demographic, clinical, treatment, and outcome data were collected for the 22 CCBD case patients identified with first incident CDI between June 1 and September 6, 2012 (Table 2). The median age was 5 years (range, 1–21 years). The most frequent comorbidities were acute lymphoblastic leukemia (n = 8; 36%), acute myeloid leukemia (n = 6; 27%), and solid

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tumors (n = 5; 23%). Hematopoietic stem cell transplantation had been performed on 7 (32%) case patients; 5 were allogeneic.

Fever was documented in 5 (23%) case patients, and most had documentation of soft, loose, or liquid stool (n = 18; 82%) in the 24 hours before their first CDPST. Neutropenia (defined as at least 1 absolute neutrophil count <500 in the prior week) was documented in 9 (41%) case patients. Eight case patients had stool tested for other pathogens (5 tested for multiple pathogens) using bacterial culture (n = 4; 18%), viral culture (n = 4; 18%), or viral electron microscopy (n = 4; 18%). Only 1 case patient had another pathogenic organism (adenovirus) ≤2 weeks before or after *C difficile* diagnosis.

Of the 18 case patients with diarrhea, 17 had documented resolution of diarrheal symptoms (≤3 unformed stools for 2 consecutive days or symptom improvement noted by clinician) by 2 days after treatment completion. No serious adverse outcomes, including admission to an intensive care unit, colectomy, or death during hospitalization or before the next outpatient visit, were noted.

Case-control study

In the bivariable analysis (Table 3), cases were more likely than controls to have prior hematopoietic stem cell transplantation, more inpatient hospital days in the prior 4 weeks, hospitalization in the BMT ward in the prior 4 weeks, exposure to any antimicrobial and several specific antibiotic classes in the prior 12 weeks, exposure to any gastric acid suppression in the prior 4 weeks, and exposure to an H2 blocker in the prior 12 weeks.

Interviews were conducted among 18 case patients and 40 controls. Compared with the controls, cases used the BMT ward kitchen and family bathroom and family rooms on other floors significantly more often (Table 3).

In the multivariable logistic regression (Table 3), cases were more likely than controls to have had exposure to cefepime or a computerized tomography (CT) scan in the prior 12 weeks or hospitalization in the BMT ward in the prior 4 weeks. Variables from interviews were not included in the model because of the lower numbers of patients captured in the interviews.

Infection prevention assessment

Inconsistent hand hygiene practices were noted among family members and staff on the CCBD overflow inpatient ward. In the outpatient setting, some breaches in personal protective equipment use were observed for patients on contact precautions, including occasional use of the same gown and gloves in multiple patient rooms and inconsistent hand hygiene on entering and exiting rooms. Although environmental cleaning appeared consistent with hospital policy, computer keyboards used by multiple staff in the clinic were not cleaned by either environmental services or clinical staff.

Environmental sampling

From September-October 2012, 71 environmental samples were collected from the CCBD inpatient ward and outpatient clinic (Supplemental Table 1). *C difficile* was isolated

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from only 1 sample: the examination table in an outpatient exam room before cleaning. The isolate was indistinguishable from that of a persistently colonized case patient (asymptomatic 51 days post-CDI diagnosis) who used the table 2 hours prior to sampling.

Antimicrobial prescribing assessment

Total antimicrobial use rates among CCBD patients did not increase during the study period; however, use from month to month varied widely (Fig 4). Ceftazidime use decreased starting in June 2011, whereas cefepime use increased and remained elevated throughout 2012, reflecting a hospital shift in empirical treatment for neutropenic fever from ceftazidime to cefepime, consistent with recent published guidelines.[7]

Isolate typing and analysis

Twenty-two *C difficile* isolates from 17 patients and the clinic examination table were tested at the CDC. Nine isolates were from 7 case patients in the June-August cluster; 4 of these patients had isolates from the initial time of diagnosis (of which 2 had a follow-up isolate 27–31 days after initial diagnosis), and 3 had isolates from 49–93 days after diagnosis. The remaining 12 isolates were collected from 10 patients who had CDI outside of the June-August cluster.

There were 12 distinct PFGE types among the 22 isolates (Supplemental Table 2). Five PFGE types were identified among the 7 case patients tested who were part of the June-August cluster; 2 case patients had the North American PFGE type 4 strain, the same strain found on the clinic examination table used by 1 of the case patients 51 days after CDI diagnosis; and 2 case patients had an identical unnamed strain type. Two case patients had serial isolates matching their initial diagnosis strain, whereas another patient had a different strain type after 1 month.

Interventions and follow-up

At the conclusion of the investigation, infection prevention interventions included reinforcement of previously implemented measures (Table 1) and new policies emphasizing routine handwashing for families and patients, terminal cleaning of common areas after use by patients with diarrhea, and continued CDI surveillance. No targeted antimicrobial stewardship interventions occurred, and cefepime remained as first-line empirical treatment of neutropenic fever. HO CDI rates subsequently decreased to an average of 19.1 per 10,000 patient days from September 2012-August 2013.

DISCUSSION

This report describes an investigation of an increase in CDI among hospitalized children in an oncology setting. The increase was seen primarily in HO CDI, and independent risk factors for infection included exposure to cefepime, the BMT ward, and CT scanning. A wide diversity of strain types was found in this population; however, few isolates were available from incident cases during the June-August 2012 CDI cluster. HO CDI rates returned to near-baseline levels with enhanced infection prevention measures, including environmental cleaning and prolonged contact isolation.

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The investigation found a specific association between CDI and cefepime, raising the question of whether the increase in CDI was partially attributable to the shift from using ceftazidime to cefepime for patients with neutropenic fever, in line with recent guidelines.[7] Because this case-control study did not include subjects before and after this shift in antimicrobial use, this hypothesis could not be assessed. However, other studies in adult and pediatric cancer populations have implicated cefepime over other antimicrobials as being associated with greater CDI risk.[4,8] More research to evaluate the potential role of shifting empirical therapy to cefepime on CDI risk is needed.

An accompanying investigation found 20 of 33 (61%) CCBD patients with prior CDI were intermittently positive for *C difficile* by PCR or culture in the 20 weeks after treatment, with or without diarrhea.[6] Based on whole genome sequencing analysis, 3 of 5 patients with multiple positive tests after their incident CDI carried different strain types at sequential time points.[6] Acquisition of new strain types and persistent colonization are likely related to disruption of the intestinal microbiota through exposure to antimicrobials, chemotherapy, and acid suppression, with subsequent acquisition of *C difficile* spores from intensive health care exposures. Dominguez et al found 0 of 11 patients with a new oncologic diagnosis were colonized with *C difficile* compared with 10 of 34 (29%) established CCBD patients.[6] Given the high prevalence of colonization in this population, strategies to reduce patient susceptibility to CDI through limitation of predisposing factors are needed.

The variety of strain types raises questions about potential sources and modes of *C difficile* acquisition. The increase in HO cases and the significant associations with hospital location (eg, BMT ward, kitchen, family bathroom) suggest hospital acquisition occurred, either indirectly or directly from other patients. A recent U.K. study found only about a third of CDI cases in a region could be traced to a symptomatic patient serving as a source of transmission, suggesting a role of other sources, including asymptomatically colonized patients or environmental reservoirs.[9] Our environmental sampling demonstrated an asymptomatic prior CDI case could shed *C difficile* into the clinic setting 51 days after diagnosis, supporting this hypothesis.

This investigation revealed several infection control challenges in the pediatric population. Compliance with contact precautions and restrictions on access to common spaces was challenging during prolonged hospitalizations. Furthermore, family members who frequently move from patient rooms to common areas without strict adherence to hand hygiene could facilitate spread of *C difficile*. Inclusion of patients and family members in educational and auditing efforts and attention to environmental cleaning of common areas should be emphasized. Despite these challenges, a reduction in HO infections to near-baseline levels was observed after implementation of enhanced infection prevention measures. However, HO infections (19.1/10,000 patient days) remained above most recent national averages in this population (13.4/10,000 patient days).[4]

Exposure to the CT scans was an unanticipated risk factor for CDI on analysis of the case-control study data; therefore, no environmental sampling of the CT scanner was performed. A subsequent review by hospital staff did not identify infection control breaches related to this procedure. However, the potential for *C difficile* acquisition from sources other

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than the hospital ward is supported by the recent genomic study in the United Kingdom, demonstrating that 36% of patients with CDI genetically related to prior infections had no known hospital ward or community contact with a previous case.[9] Further research is needed to identify these unknown risk factors.

This investigation had several limitations. First, the clinical presentation of CDI in this population was mild and difficult to distinguish from other common causes of diarrhea, including antimicrobial and chemotherapy exposure. However, we found no evidence of changes in testing practices at the start of the outbreak, and most patients showed resolution of diarrhea on *C difficile* treatment, suggesting these were true, albeit mild, infections. PCR diagnostic testing is also more likely to lead to detection of mild CDI or cases of colonization in patients with diarrhea because of other causes.[10] However, the use of more sensitive testing methods may be an important strategy for interrupting transmission. Given the potential difficulty in distinguishing between colonization and infection in this population, the decision to treat CDI should be based on clinical factors in addition to testing. We were also limited in evaluating transmission during the outbreak period because *C difficile* isolates were only available for 4 case patients from the time of initial diagnosis, none of whom was diagnosed in June, when hospital-associated transmission was most likely. Finally, environmental sampling was performed >2 months after the initial increase in CDI and after changes were made in environmental cleaning practices; therefore, our sampling likely does not reflect the period most concerning for health care transmission.

In conclusion, an increase in CDI occurred among patients in a pediatric oncology setting. Although epidemiologic evidence suggests a role of health care transmission, the wide variety of strain types in this population suggests the possibility of multiple sources of acquisition. Further study is needed to understand the role of colonized patients in transmission and strategies to reduce CDI risk through limiting alterations of the intestinal microbiota. In particular, studies examining potential unintended consequences of adopting cefepime for primary treatment of neutropenic fever are needed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Disclaimer:

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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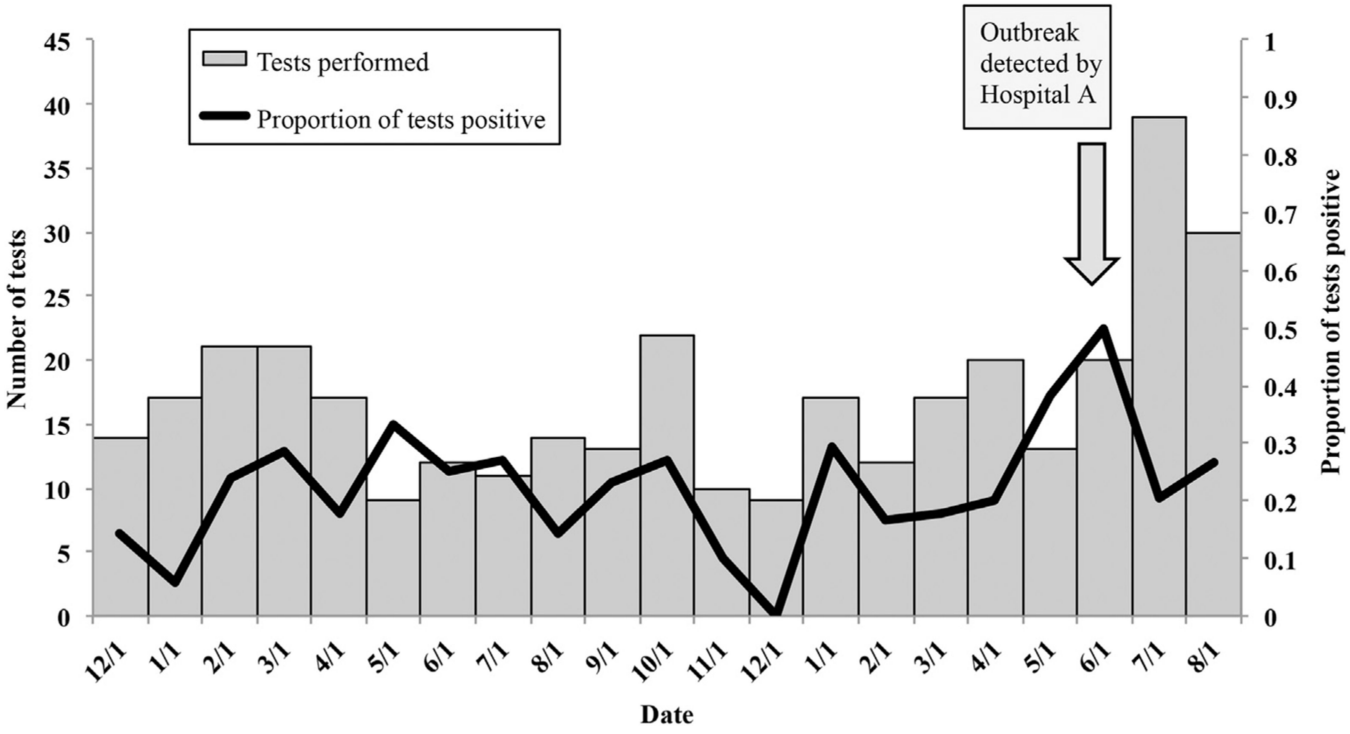

Fig 1.

Results of *Clostridium difficile* diagnostic tests ordered among the Center for Cancer and Blood Disorders patients, December 1, 2010-August 29, 2012 (N = 358).

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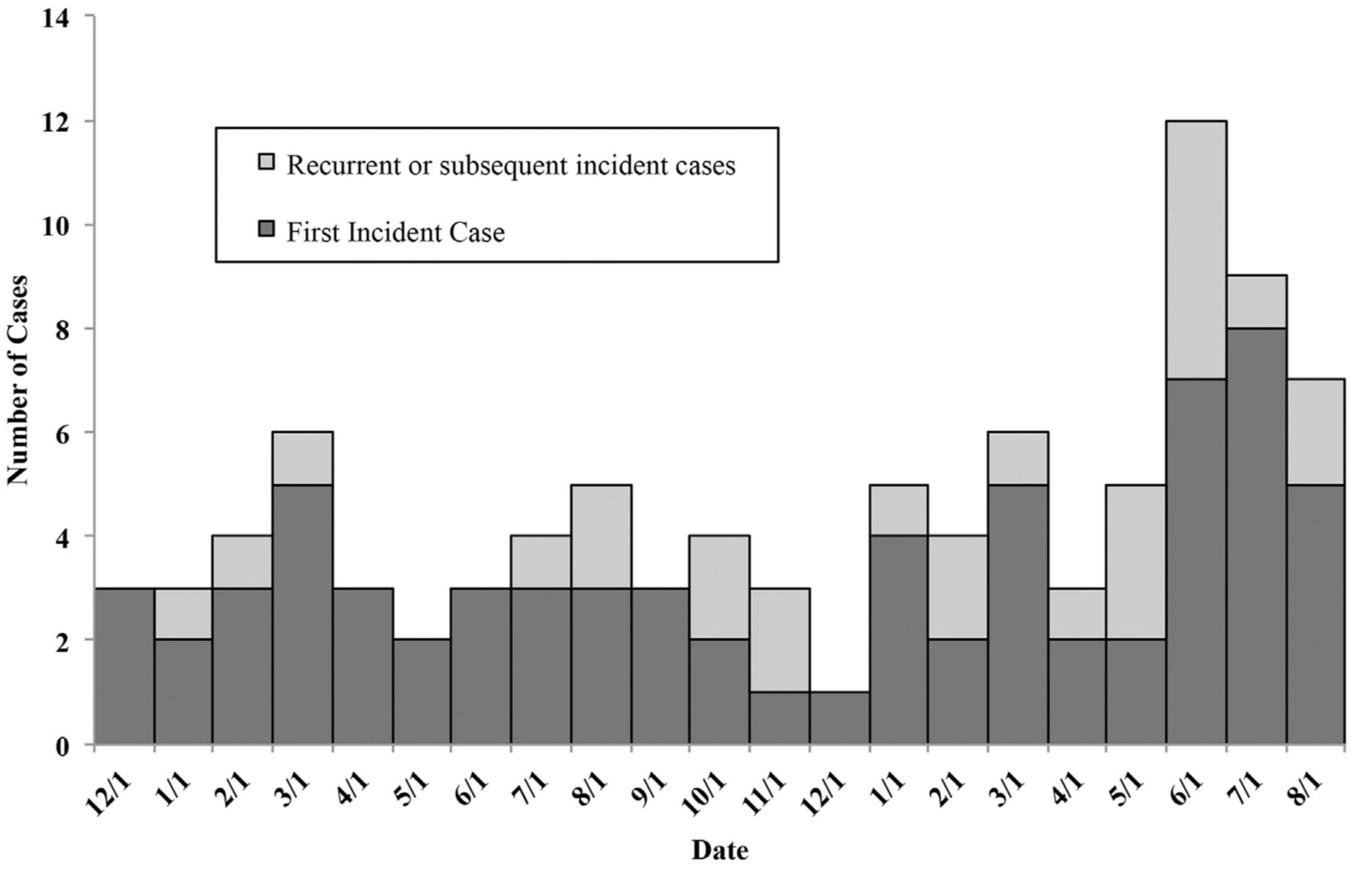

Fig 2.

Cases of *Clostridium difficile* among the Center for Cancer and Blood Disorders patients, stratified by case type, December 1, 2010-August 29, 2012 (n = 95).

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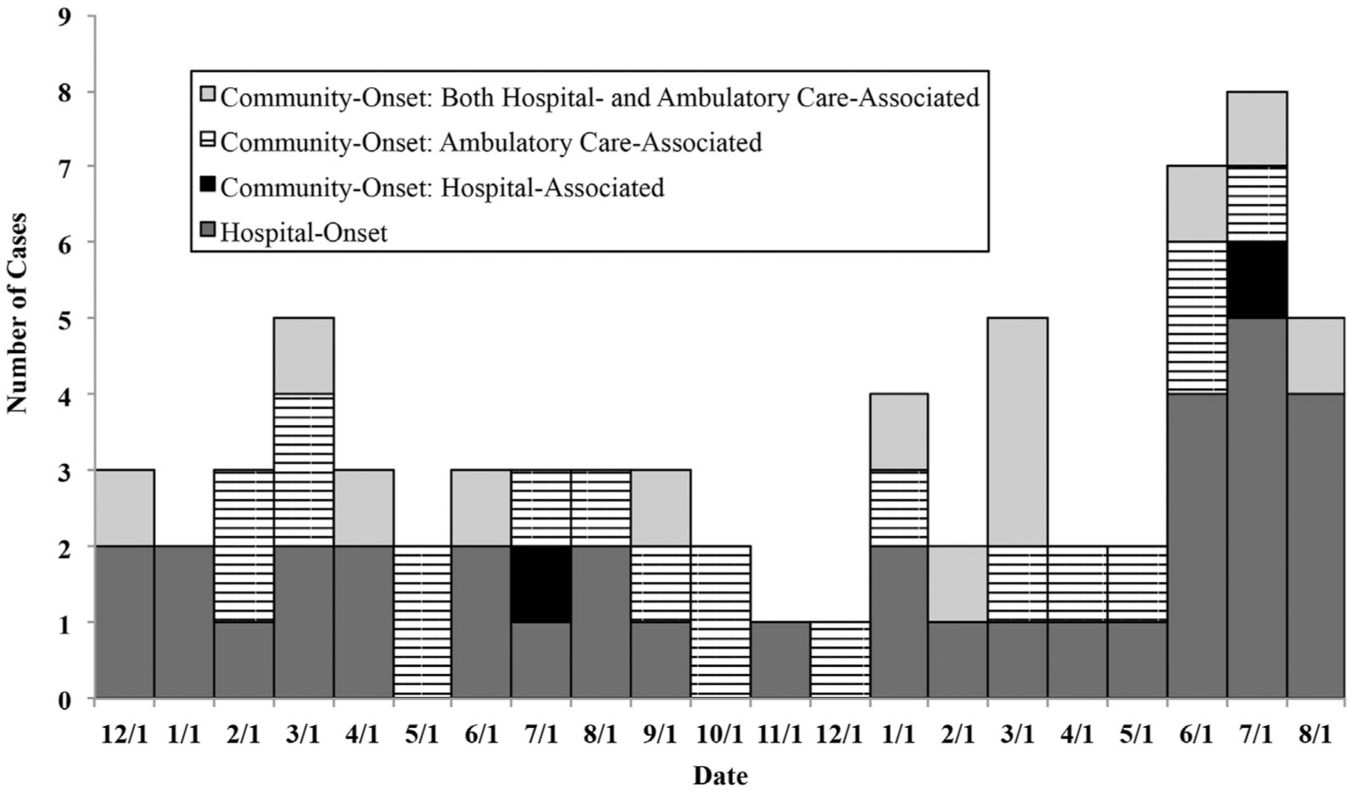

Fig 3.

First incident cases of *Clostridium difficile* in the Center for Cancer and Blood Disorders patients, stratified by hospital-versus community-onset cases, December 2010-August 19, 2012 (n = 69).

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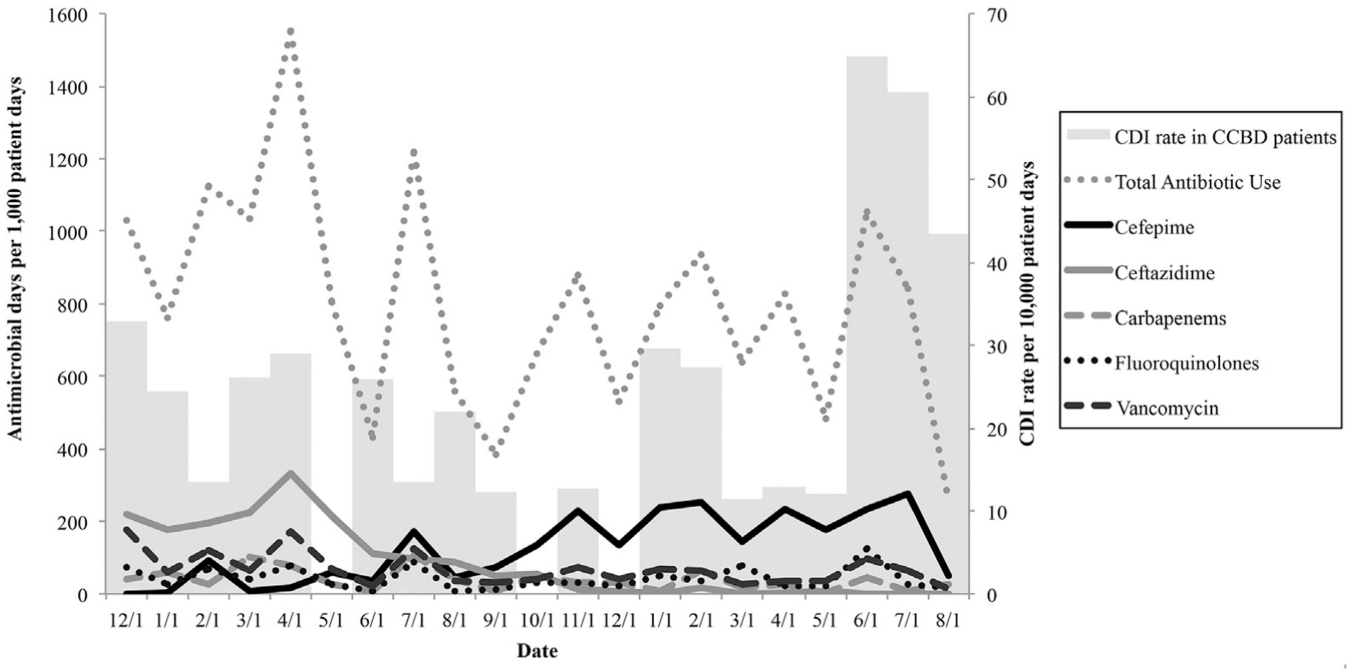

Fig 4.

Select antimicrobial use and hospital-onset *Clostridium difficile* infection (CDI) rates among the Center for Cancer and Blood Disorders (CCBD) patients, December 2010-August 2012.

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Table 1

Infection prevention policies implemented immediately before CDPHE-CDC investigation

Category	Intervention
Environmental cleaning	• Universal sodium hypochlorite (1:10 solution) disinfection in all CCDB areas instead of just contact isolation rooms. • Increased frequency of environmental cleaning to 2–3 times daily and between each patient in outpatient clinic. • Cleaning of family lounge after each family use.
Personal protective equipment	• Universal glove use. • Continue contact precautions for all patients with current or prior CDI.
Isolation policies	• Closure of playrooms. • Restriction of family lounge to a single family at a time. • Cessation of group and communal gathering activities for CCBD patients and families. • Family education regarding hand hygiene and other infection control policies. • Dedicated patient equipment in each room (eg, medication barcode scanners, scales, stethoscopes). • Electronic alert for providers in medical records for all patients with CDI. • Storage of multidose containers (eg, nasal spray) in individual plastic bags in shared refrigerator for individual patients in isolation.

CCBD, Center for Cancer and Blood Disorders; *CDC*, Centers for Disease Control and Prevention; *CDI*, *Clostridium difficile* infection; *CDPHE*, Colorado Department of Public Health and Environment.

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Table 2

Characteristics of Center for Cancer and Blood Disorder case patients (n = 22) with first incident *Clostridium difficile* infections identified between June 1-September 6, 2012

Characteristic	Value
Demographics	
Male sex	14 (64)
Age (y)	5 (1–21)
Age <2 y	3 (14)
Race	
White	15 (68)
Black	1 (5)
Other-unknown	6 (23)
Ethnicity	
Hispanic	9 (41)
Non-Hispanic or unknown	13 (59)
Non-Hispanic white	11 (50)
Hematologic malignancy, any	15 (68)
Acute myeloid leukemia	6 (27)
Acute lymphoblastic leukemia	8 (36)
Lymphoma	1 (5)
Solid malignancy, any	5 (23)
Hematopoietic stem cell transplant	7 (32)
Allogenic stem cell transplant	5 (23)
Autologous stem cell transplant	2 (9)
Solid organ transplant	1 (5)
Primary immune deficiency	1 (5)
Down syndrome	1 (5)
Clinical presentation	
Fever	5 (23)
Stool description in 24 h before positive *Clostridium difficile* test	
Soft	3 (14)
Loose	8 (36)
Liquid	7 (32)
No description	4 (18)
≥3 stools documented	11 (50)
Days of diarrhea before positive *C difficile* test	1 (1–4)
Neutropenia	
Cases with absolute neutrophil count <500 in prior week	9 (41)
Abnormal abdominal imaging ≤5 d of *C difficile* diagnosis	2 (9)
Location 4 d before incident *C difficile* stool	
CCBD hematology-oncology ward	6 (27)
CCBD bone marrow transplant ward	4 (18)

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Characteristic	Value
Other inpatient unit	2 (9)
Home	7 (32)
Unknown	3 (14)
Location of first positive *C difficile* stool collection	
CCBD hematology-oncology ward	8 (36)
CCBD bone marrow transplant ward	6 (27)
Other inpatient unit	3 (14)
Outpatient CCBD clinic including infusion center)	2 (9)
Unknown	3 (14)
Admitted for *C difficile* infection	3 (14)
Other stool diagnostic tests within 24 h of positive *C difficile* test	
Bacterial culture	4 (18)
Viral culture	4 (18)
Viral electron microscopy	4 (18)
Cases with positive stool tests for non-*C difficile* pathogen adenovirus)	1 (5)
C difficile infection treatment	
Metronidazole, oral	15 (68)
Metronidazole, oral and intravenous	5 (23)
Metronidazole, oral and vancomycin, oral	1 (5)
Metronidazole, intravenous and vancomycin, oral	1 (5)
Duration of treatment	10 (7–12)
Outcomes	
Resolution of diarrhea 2 d after completion of treatment *	17 (94)
Adverse event (transfer to intensive care, colectomy, or in-hospital death)	0 (0)

NOTE. Values are n (%) or median (range).

CCBD, Center for Cancer and Blood Disorders.

* n = 18.

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Table 3

Risk factors associated with first incident *Clostridium difficile* infection identified between June 1 and September 6, 2012, among Center for Cancer and Blood Disorder patients

Characteristic	Case patients (n = 22)	%	Control patients (n = 60)	%	Unadjusted OR (95% CI)	*P* value	Adjusted OR (95% CI)	*P* value
Demographics								
Acute myeloid leukemia	6	27	7	12	2.84 (0.83–9.67)	.095		
Solid malignancy, any	5	23	28	47	0.34 (0.11–1.03)	.056		
Stem cell transplant, any	7	32	5	8	5.13 (1.43–18.50)	.012		
Allogenic stem cell transplant	5	23	4	7	4.12 (0.99–17.08)	.051		
Absolute neutrophil count <100 in prior week	8	36	8	13	2.79 (0.88–8.84)	.082		
Health care exposures								
Median inpatient days in prior 4 wk (range)	9.5 (1–28)		5 (0–27)			.006		
CCBD BMT ward in prior 4 wk	7	32	3	5	8.87 (2.04–38.46)	.004	18.28 (2.54–131.71)	.004
Computerized tomography scan in prior 12 wk	8	36	10	17	2.86 (0.95–8.61)	.062	5.20 (1.23–22.07)	.025
Lumbar puncture in prior 12 wk	14	64	25	42	2.45 (0.89–6.72)	.082		
BMT kitchen, Likert scale mean (range) [*,†]	2 (1–5)		1.2 (1–4)			.034		
BMT hallway family bathroom, Likert scale mean (range) [*,†]	2 (1–5)		1.1 (1–4)			.005		
Family rooms outside CCBD floor, Likert scale mean (range) [*,†]	1.8 (1–5)		1.2 (1–4)			.004		
Medications								
Any antimicrobial prior 12 wk	22	100	54	90	∞			
Cephalosporin, any in prior 12 wk	22	100	46	77	∞			
Cephalosporin, 3rd or 4th generation in prior 12 wk	21	95	35	58	15.00 (1.89–118.96)	.010		
Cefepime in prior 12 wk	19	86	30	50	6.33 (1.69–23.68)	.006	14.11 (2.53–78.65)	.003
Vancomycin in prior 12 wk	11	50	15	25	3.00 (1.08–8.32)	.035		
Antifungal in prior 12 wk	11	50	17	28	2.53 (0.92–6.92)	.071		
Any gastric acid suppression in prior 4 wk	19	86	37	62	3.94 (1.05–14.80)	.043		
Histamine 2 antagonist in prior 12 wk	20	91	40	67	5.00 (1.06–23.55)	.042		

BMT, bone marrow transplant; *CCBD*, Center for Cancer and Blood Disorders; CI, confidence interval; *OR*, odds ratio.

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[*] Variable not included in multivariable model because of lower participation (18 cases, 40 controls).

[†] Likert scale for frequency of use: 1 (never), 2 (once per week or less), 3 (occasionally (2–5 times per week), 4 (daily), and 5 (multiple times per day).