

Ramesh V. Nathan, MD¹; Barry Statner, MD¹; Philip S. Brachman, MD²; Andrew H. Krinsky, MD³; Robin H. Dretler, MD⁴; Lucinda J. Van Anglen⁵, PharmD

¹Mazur, Statner, Dutta, Nathan, PC, Thousand Oaks, CA; ²Atlanta ID Group, PC, Atlanta, GA; ³Infectious Diseases Associates, Sarasota, FL;

⁴Infectious Disease Specialists of Atlanta, Atlanta, GA; ⁵Healix Infusion Therapy, Inc., Sugar Land, TX

Ramesh V. Nathan, MD
Mazur, Statner, Dutta, Nathan, PC
2220 Lynn Rd, Ste 301
Thousand Oaks, CA 91360
(805) 495-1073
nathanmd@yahoo.com

Abstract

Background: Hospitalization, antibiotic use, age>65 yrs, and use of proton pump inhibitors (PPI) are significant risk factors for development of *C. difficile* infection (CDI) [1]. Patients (pts) receiving intravenous antibiotics (IVAB) in a POIC have reduced hospital exposure; therefore pts may have a lower risk of developing health care facility-associated CDI with a decreased incidence of recurrence.

Methods: We retrospectively reviewed 1,352 pts treated at 9 Infectious Disease POICs with IVAB from January 1 to June 30, 2011. Evaluable pts received one or more doses of IVAB at the POIC, were diagnosed with CDI while receiving care through the POIC, and had a 90 day follow-up. Database analysis included demographics, antimicrobial use, including oral and IV drugs, evidence of confirmed or suspected CDI, and subsequent treatment, incidence, outcomes and recurrences.

Results: During the 6-month study period, 1,352 pts were seen at 9 participating POICs. 14 cases (1%) of confirmed or suspected CDI were documented. The mean age was 60 yrs, with 6 pts (43%) ≥ 65 yrs. Location prior to POIC admission was a hospital in all pts. Based on surveillance definitions, 10 pts met criteria for community onset-health care facility associated CDI and 4 were indeterminate. PPI were used in 4 pts (29%) and probiotics in 6 pts (43%), 4 of whom began therapy prior to onset of diarrhea. Case pts received a total of 33 antibiotics. Ceftriaxone and vancomycin were the most causative agents (5/14 pts each), with cephalosporins causative in 9 of 14 pts (64%). The incidence of CDI for pts treated at POICs was 2.9 per 10,000 pt-days. Treatments for CDI were oral metronidazole (n=10, 71%), probiotics only (n=1, 7%), monitoring (n=1, 7%) and anti-diarrheal medications (n=2, 14%). One pt experienced an AE related to metronidazole with resolution upon discontinuation. Successful outcomes were achieved in all but one pt who was lost to follow up (93%). No recurrences were observed.

Conclusion: Rates of CDI were low in pts receiving IVAB at POICs. Treatment of CDI was successful with no recurrence in the POIC setting, even with health care facility associated onset. This study further validates the safety of transitioning appropriate pts from an inpatient setting to a POIC for continued IVAB therapy.

Introduction

CDI is a leading cause of nosocomial infections, with disease severity ranging from mild diarrhea to fulminant colitis [1]. Interestingly, *C. difficile* can be found on 49% of surfaces in hospital rooms occupied by pts with CDI [2]. The incidence, severity as well as morbidity, mortality and economic burden associated with CDI has been on the rise over the last decade [3]. This is thought to be at least partially due to frequent antibiotic use and various host factors such as advanced age, prior hospitalization, use of PPIs and severity of underlying illnesses [1-4].

Nearly all antimicrobial classes have been associated with CDI, however, clindamycin, third-generation cephalosporins and penicillins have been considered to harbor the greatest risk [4]. Based on standardized surveillance data, the overall incidence rate of CDI in the U.S. ranged from 7 to 8.5 cases per 10,000 pt-days in health care facilities [3]. Recently, it has been demonstrated that pts receiving IVAB therapy at POICs tend to have shorter hospital stays and may be less likely to acquire CDI [5].

Our research objective was to report risk factors, treatment, incidence, outcome and recurrences of CDI in pts receiving IVAB at participating POICs across the U.S.

Methods

A multicenter retrospective database and chart review was conducted to identify all pts who received at least one intravenous antibiotic (IVAB) in 9 POICs nationally. Data on demographic information of 14 pts categorized into 2 groups, confirmed and suspected CDI, were collected.

Inclusion Criteria:

- Pts ≥ 18 yrs receiving any IVAB at a participating POIC from January 1 to June 30, 2011
- Pts with confirmed or suspected *C. difficile*
- Pts with 90 day follow-up data available

Clinical Definitions:

- Confirmed CDI: ≥ 3 diarrhea episodes in ≤ 24 hrs AND either a positive stool test for *C. difficile* or its toxin OR a colonoscopic/histopathologic finding demonstrating pseudomembranous colitis
- Suspected CDI: presence of ≥ 2 diarrhea episodes within 24 hr period
- CDI case definitions were made based upon SHEA and IDSA Clinical Practice Guidelines
- Recurrence: 2nd episode of *C. difficile* infection within 60 days after the first episode
- IVAB use data were collected for the 2-month period leading up to CDI diagnosis

Outcomes Definitions:

Cured: clinical signs and symptoms resolved with no further treatment necessary; Improved: partial resolution of clinical signs and symptoms; Failed: no resolution of signs and symptoms; Non-evaluative: patient lost to follow-up or transferred elsewhere

Data Analysis:

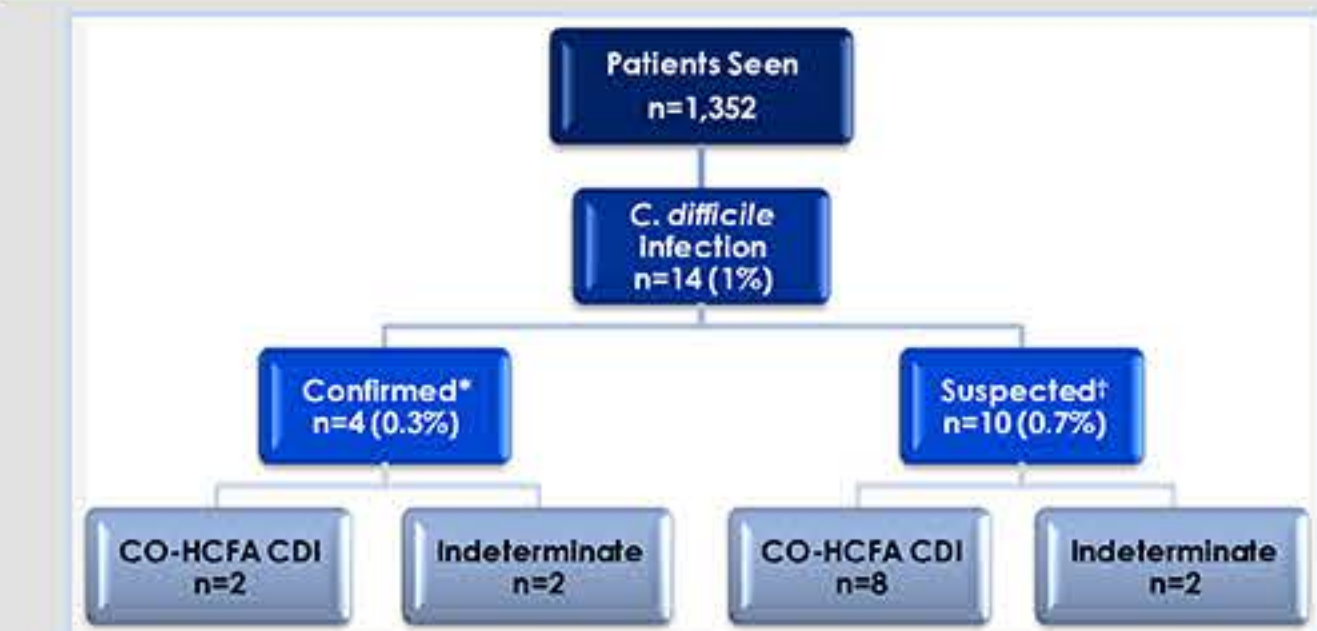
- Descriptive statistics (mean) were used for demographic data.
- Incidence rates were expressed as number of pts in POICs per 10,000 pt-days and compared to a multicenter study of national CDI rates from 2000 to 2006 [3].

Results

Study Characteristics and Demographics

- 1,352 pts were seen at 9 participating POICs.
- 14 CDI patients including 4 confirmed and 10 suspected were documented.

Figure 1. CDI Characteristics



*: Confirmed: stool sample positive for *C. difficile* or its toxin, †: Suspected: symptomatic diagnosis. CO-HCFA: Community Onset-Health Care Facility Associated.

Table 1. Demographics

Characteristics	Confirmed CDI (n=4)	Suspected CDI (n=10)
Gender		
Female	3	2
Male	1	8
Age (years)		
Mean (range)	69 (59-75)	56 (22-79)
≥ 65	3	3
< 65	1	7
BMI (kg/m²)		
Mean (range)	31 (29-36)	25 (18-40)*
≥ 30	1	1
Co-morbidities		
Diabetes	4	2
Hypertension	3	2
Immunocompromised State	1	5
Hyperlipidemia	0	1
Other [†]	3	2
Co-morbidities per Patient		
0	0	2
1	0	2
2	4	5
≥ 3	3	3
Prior hospitalization (days)		
Mean (range)	13 (4-22)	6 (2-11)
PPI Use (No. of pts)	0	4
Probiotic Use (No. of pts)	0	6
Start prior to diarrhea onset	0	4
Start after diarrhea onset	0	1

*Based on data for 9 pts, †Other co-morbidities included anxiety/depression, cardiac disease, hypothyroidism, osteoarthritis, renal insufficiency, and rheumatoid arthritis.

- Pts with confirmed CDI tended to be older than pts with suspected CDI; however, suspected CDI pts were more likely to use PPIs (n=4) and probiotics (n=6); four of whom began therapy prior to onset of diarrhea.
- Potential risk factors such as previous hospitalization, ≥2 antibiotics for a duration of ≥22 days, age >59 years, and ≥2 co-morbidities were reported in 100% of pts with confirmed CDI cases.
- 100% of pts with confirmed CDI were previously hospitalized and received at least 2 antibiotics prior to their CDI diagnosis.

Antimicrobial Utilization in CDI Patients

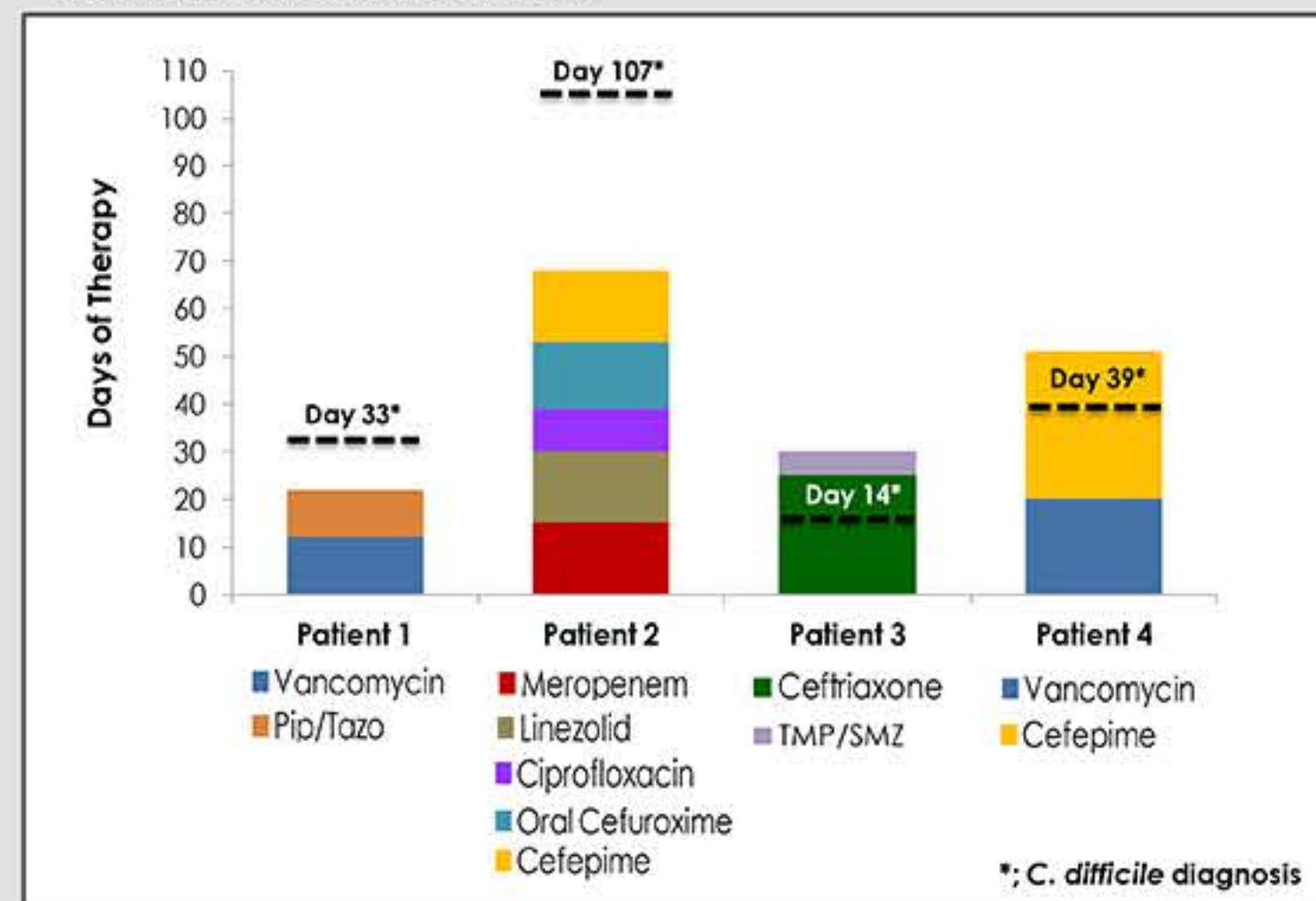
Table 2. Admitting Diagnosis and Antimicrobial Use

Pt. Number	Admitting Diagnosis	Antimicrobial Usage	
Confirmed CDI	1	Pneumonia	Vancomycin, Piperacillin-Tazobactam
	2	Pneumonia, UTI	Meropenem, Linezolid, Ciprofloxacin, oral Cefuroxime, Cefepime
	3	Knee infection (post-operative)	oral Sulfamethoxazole-Trimethoprim, Ceftriaxone
	4	Diskitis	Vancomycin, Cefepime
Suspected CDI	5	Bacteremia, UTI	Ceftriaxone
	6	Lung abscess	Doripenem, Ceftriaxone
	7	Pneumonia	Piperacillin-Tazobactam
	8	Osteomyelitis	Vancomycin, Cefazolin, Daptomycin, oral Cephalixin
	9	Diabetic foot infection	Ceftriaxone
	10	Osteomyelitis	oral Ciprofloxacin, Ceftriaxone
	11	Diabetic foot infection	Vancomycin, Piperacillin-Tazobactam
	12	Cellulitis	Vancomycin, Piperacillin-Tazobactam
	13	Bacteremia	oral Sulfamethoxazole-Trimethoprim, oral Levofloxacin, Gentamicin, Cefepime
	14	UTI	oral Ciprofloxacin, Gentamicin, Aztreonam

- The median number of antimicrobials used in confirmed: suspected CDI pts was 2.5:2.
- Third-(ceftriaxone) and fourth-(cefepime) generation cephalosporins were the most often used antibiotics (8/14 pts).

Figure 2. Antimicrobial Use and CDI Onset

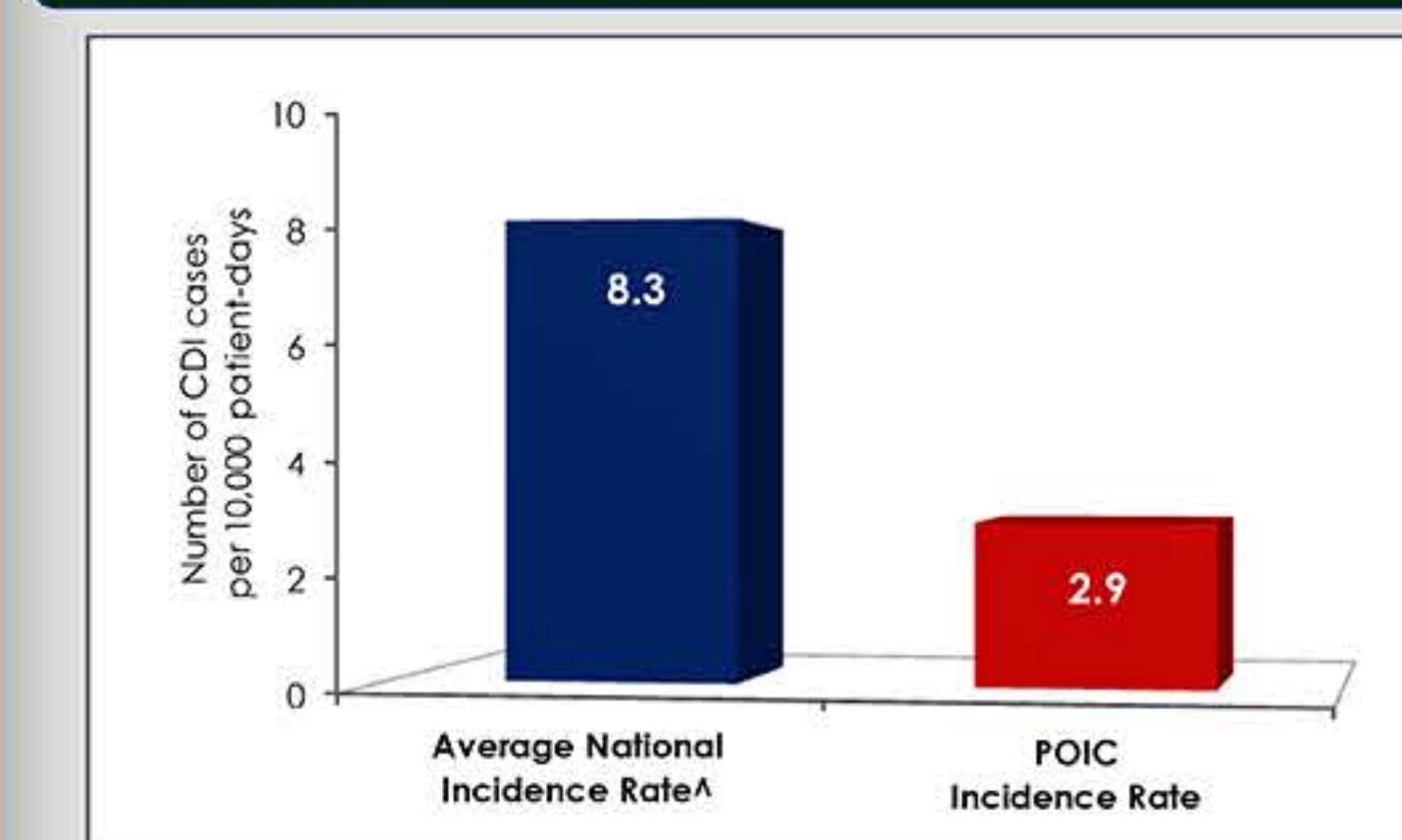
Confirmed CDI Patients:



- The median duration of antimicrobial use in confirmed CDI pts was 40 days (range: 22-68 days) with a median duration for CDI onset of 36 days.
- The most common used IVAB in confirmed CDI pts was cefepime (2/4 pts).

Incidence Rate and Therapy of CDI

Figure 3. CDI Incidence



△: Dubberke ER et al. "Multicenter study of CDI rates from 2000 to 2006" [3].

- The average incidence rate of health care associated CDIs in the US, including 5 medical centers, was 8.3 cases per 10,000 pt-days [3].
- In comparison, the CDI incidence rate for pts treated at 9 POICs was 2.9 cases per 10,000 pt-days; a 65% reduction compared to national average.

Table 3. Therapy, Outcome, and Recurrence

Patient Number	Type of CDI	Treatment	Length of Therapy (days)	Final Outcome	Recurrence
Confirmed Patients					
1	CO-HCFA ¹	MTZ ² 500 mg TID	14	n/a ³	None
2	Indeterminate	MTZ 500 mg TID	14	Cured	None
3	CO-HCFA	MTZ 250 mg QID	19	Cured	None
4	Indeterminate	MTZ 500 mg TID	14	Cured	None
Suspected Patients					
5	CO-HCFA	MTZ 500 mg QID	10	Cured	None
6	CO-HCFA	Loperamide	n/a	Cured	None
7	CO-HCFA	Probiotics	12	Cured	None
8	Indeterminate	Loperamide	n/a	Cured	None
9	CO-HCFA	Monitoring	n/a	Cured	None
10	CO-HCFA	MTZ 500 mg TID	2	Cured	None
11	Indeterminate	MTZ 500 mg TID	10	Cured	None
12	CO-HCFA	MTZ 500 mg TID	10	Cured	None
13	CO-HCFA	MTZ 500 mg TID	n/a	Cured	None
14	CO-HCFA	MTZ 250 mg QID	7	Cured	None

¹ CO-HCFA: Community Onset-Health Care Facility Associated, ² MTZ: Metronidazole ³ n/a: not available.

- Treatment for CDI was initiated on average 2 days following the first episode of diarrhea.
- Pts with confirmed CDI tended to receive a longer MTZ treatment course than pts with suspected CDI (mean: 15.2 vs. 8.5 days).
- One pt treated with MTZ experienced low grade fever and sore throat (low severity) which resolved upon MTZ discontinuation.
- At completion of therapy, 13 pts (93%) were evaluated as cured while one pt was non-evaluative due to loss of follow-up.
- There were no recurrences in either group at the 60 day follow-up after the first CDI episode.

Discussion

Recent studies have shown that the incidence and severity of CDI in healthcare facilities are increasing in the U.S. [1-3]. People most at risk for CDI are older adults, who take multiple antimicrobials and are hospitalized or in long term care facilities [4, 5].

In this retrospective study, a total of 1,352 pts in 9 POICs across the U.S. were reviewed on demographic information, antimicrobial use, CDI incidence, therapy, outcome and recurrences within the defined study period. The objectives of this study were to describe the most likely affecting antibiotic(s) causing CDI, as well as incidence and outcome of CDI in POICs.

Pts identified with CDI were presented with a variety of diagnosis and characteristic risk factors such as prior hospitalization, ≥ 2 co-morbidities, multiple antimicrobial usage, and mean age ≥ 56 yrs. The most utilized IV antimicrobials in patients with suspected or confirmed CDI were ceftriaxone (36%), vancomycin (36%) and piperacillin-tazobactam (29%). In fact, third- and fourth-generation cephalosporins were utilized in nearly 60% of CDI pts in this study.

We report a low rate of combined suspected and confirmed CDI in the POIC population; 2.9 per 10,000 pt-days. In comparison, the average incidence rate of health care-associated CDIs obtained from 5 medical centers across the U.S. was 8.3 cases per 10,000 pt-days, indicating an approximately 3-fold reduction of CDI cases in the POIC group. Pts were treated with metronidazole, loperamide, or probiotics resulting in 93% cure rate with one patient lost to follow-up. Importantly, no recurrences were reported within 60 days after the first episode of CDI.

Conclusion

- 1,352 pts were seen at 9 POICs with 4 confirmed (0.3%) and 10 suspected (0.7%) cases of CDI.
- Pts with confirmed CDI tended to be older, recently hospitalized, received a longer course of antibiotics and received a longer treatment course for their CDI compared to suspected CDI patients.
- Most prescribed IVABs associated with CDI were ceftriaxone (36%), vancomycin (36%) and piperacillin-tazobactam (29%).
- Third- and fourth-generation cephalosporins were used in 8 of 14 pts overall (57%); 3 of 4 confirmed patients (75%) and 5 of 10 suspected pts (50%).
- Median duration of antimicrobial use in confirmed CDI pts was 40 days (range: 22-68) with a median CDI onset of 36 days.
- The CDI incidence rate was 2.9 for the POIC group compared to 8.3 cases per 10,000 pt-days national average of health care associated CDIs indicating a 65% reduction.
- CDI was successfully treated in 13 of 14 pts with no recurrences in POICs even with health care facility associated onset.
- Further study is indicated to determine any correlation between the patient population receiving care in the POIC setting and lower rates of CDI.

References

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