INTRODUCTION

- *Clostridium difficile* (C. difficile) is a major cause of health care associated and antibiotic associated diarrhea with an increase in hospitalizations and case fatality rates observed from 2000 to 2005 [1]. All-cause mortality related to *C. difficile* infection ranges from 6.1% to 38%. Predictors of mortality include advanced age, underlying comorbid conditions, leukocytosis and acute renal insufficiency [3].
- *C. difficile* infection has been implicated as contributing to increased morbidity and mortality [4].

RESULTS

- **Table 1. Clinical and demographic variables of study population by outcome.**
  - **Survival**
    - Age, years: 65 (51, 76)
    - Number of male patients: 1183 (66%)
    - Median [IC] Charlson Comorbidity score: 8 [5-11]
    - Number with severe extent of illness: 1207 (69%)
    - Severe *C. difficile* classification: 503 (29%)
    - Age > 60: 1442 (56%)
    - WBC > 15,000 cells/mL: 231 (9%)
    - Temperature > 38.0°C: 732 (29%)
    - Albumin < 2.5 g/dL: 144 (6%)
    - Median [IC] hospital length of stay: 12 [7-22]
    - Undergoing surgical procedure during hospitalization: 997 (40%)
    - Proton pump inhibitor use: 1063 (79%)
    - Median, Interquartile range except indicated.

- **Table 2. Anti-infective use in HAAO CDAD by outcome.**
  - Survival
    - Number of episodes with antibiotic exposure before positive *C. difficile* test: 2429 (88%) 222 (99%) p < 0.01
    - Number of episodes with antibiotic exposure after positive *C. difficile* test: 2087 (84%) 212 (95%) p < 0.001
  - Death
    - Median [IC] antibiotic days of therapy before CDAD: 9 [5-16]
    - Median [IC] antibiotic days of therapy after CDAD: 4 [1-6]
  - Mortality associated treatment of *C. difficile* 1996 (84%) 104 (74%) p < 0.01
  - Oral vancomycin treatment of *C. difficile* 455 (17%) 43 (19%) p < 0.01

CONCLUSIONS

- In a large cohort of hospital acquired, hospital onset *Clostridium difficile* associated use was more prevalent prior to onset of CDAD but was reduced in survivors. Antibiotics were discontinued more frequently in survivors (84%) compared to those who died (6%) during hospitalization.
- Severity of illness, severe classification of *C. difficile*, presence of pseudomembranes and continued antibiotic use after diagnosis of *C. difficile* were associated with increased disease severity and death. Other mortality indicators include advanced age, underlying comorbidities, leukocytosis, hypotension and a rising creatinine.
- While our findings do not establish causality, these data suggest that limiting antibiotic use after diagnosis of *C. difficile* is an important measure in managing patients diagnosed with *C. difficile*.

DISCLOSURES

- The views expressed herein do not necessarily represent those of the Intermountain Healthcare Board of Directors, and no conflicts of interest related to this study are reported.

REFERENCES


Bert K. Lopansri, MD
Eddie Stenehjem, MD, MS
Kristin Dascomb, MD, PhD
John P. Burke, MD
Intermountain Medical Center, Murray, UT; University of Utah School of Medicine, Salt Lake City, UT

**ORIGINAL ABSTRACT**

**STUDY DESIGN**

- Retrospective, case control study

**DATA COLLECTION AND ANALYSIS**

- Clinical and administrative data were collected from the Intermountain Healthcare Enterprise Data Warehouse.
  - Continuous variables were analyzed with Wincox Rank Sum Test or Student t-test and proportions were compared using Fisher’s exact test or Chi Square as appropriate.
  - Logistic regression was used to model the relationship between selected variables and all cause, in hospital mortality associated with CDAD. Two models were run: 1: severe *C. difficile* as a dichotomous variable; and 2: components of disease severity listed as individual variables.

**METHODS**

- Antibiotic exposure prior to CDAD, age and leukocytosis were not associated with death in hospital acquired CD associated diarrhea (CDAD).

**RESULTS**

- Extreme severity of illness (OR [95% CI]; 13.4 [7.6-23.4]) was associated with mortality. Limiting antibiotic exposure after diagnosis of CDAD associated diarrhea (CDAD) was defined according to the 2010 *C. difficile* clinical practice guidelines (figure) [5]. Severe CDAD was defined according to the modified University of Illinois criteria [6].

**OBJECTIVE**

- To determine predictors of death in hospital acquired CD associated diarrhea (CDAD).

**CONCLUSIONS**

- **Background:** Hypervirulent *Clostridium difficile* (CD) strains are associated with increased disease severity and death. Other mortality indicators include advanced age, underlying comorbidities, leukocytosis, hypotension and a rising creatinine. The objective of our study was to determine predictors of death in hospital acquired CD associated diarrhea (CDAD).

**METHODS:** We conducted a retrospective review of hospital acquired, hospital onset *Clostridium difficile* (CDAD) over a 10-year period (2003-2012) in an integrated healthcare network. HAHO was defined according to 2010 national guidelines. Severe CDAD was defined according to the modified University of Illinois criteria [6]. Clinical and administrative data were collected from electronic sources. Logistic regression was used to measure associations between clinical parameters and all-cause mortality during hospitalization. Variables with P < 0.1 in univariate analysis were included in the multivariable model.

**Results:** We identified 2,712 HAHO CDAD encounters in 15 hospitals (10,210,000 patient days); 223 (8.2%) of these encounters ended with death. Severe CDAD was identified in 639 (24%) survivors. Nearly all patients (98%) received antibiotics prior to CDAD; however, patients who died had more antibiotic days of therapy prior to diagnosis of CDAD (median [interquartile range]: 17 [7-19] vs. 9.0 [5-16]). Death was more frequent in patients who continued to receive antibiotics other than CD treatment after diagnosis of CDAD (9.7% vs. 2.1%, p < 0.001). Factors independently associated with mortality in the multivariable model include extreme APRDRG severity of illness (OR [95% CI]: 13.4 [7-23.4]), severe CDAD (OR [95% CI]: 1.0 [1-2.2]) and continued antibiotic use after diagnosis of CDAD (3.0 [1.0-8.8]). Treatment for CD was associated with reduced mortality (OR [95% CI]: 0.4 [0.3-0.6]). Antibiotic exposure prior to CDAD, age and leukocytosis were not associated with death in the multivariable model.

**Conclusion:** Antibiotic use before and after diagnosis of hospital onset CDAD is common. In addition to extreme severity illness and severe classification of CD, continued use of non-CD antibiotics after CDAD diagnosis was associated with mortality. Limiting antibiotic exposure after diagnosis of CDAD is essential for managing patients infected with CDAD.