Extra-Intestinal *Clostridioides difficile* Infection: A Multi-Center Retrospective Review

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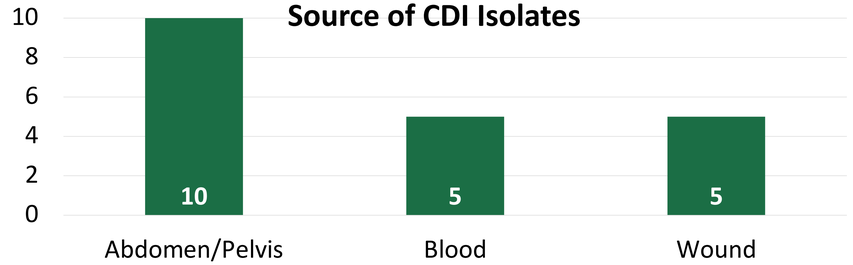
Introduction

Clostridioides difficile infection (CDI) is the most common healthcare-associated infection in the United States. The overwhelming majority of CDI cases are localized within the colon. In rare cases, however, CDI may involve locations outside the colon. There are a small number of studies reporting extra-intestinal CDI (EiCDI) and most emanate from Europe. The most recent United States study was published in 2014 from a rural healthcare setting. In this study we report on our experience with EiCDI within an urban environment at Yale-New Haven Health System (YNHHS).

Methods

We performed a retrospective descriptive analysis reviewing all patients with EiCDI at a large multi-center health system from 1/2013 until 9/2021. We electronically screened all cultures done at YNHHS regardless of the source and retrieved those that isolated *C. difficile* from an extraintestinal source (EiCDI). Data collected for each patient included demographics, medical co-morbidities, source of culture, treatment and outcomes.

Results



Demographics (N=20)	
Age, mean ± SD (years)	57.2 ± 16
Male, n (%)	11 (55%)
Race, n (%)	
Caucasian	15 (75%)
African American	3 (15%)
Asian	1 (5%)
Other	1 (5%)
Charlson comorbidity index, median [IQR]	4 [1.50, 7.25]
Hospitalization in the last 12 weeks	14 (70%)
Associated *C difficile* colitis	5 (25%)
Antibiotic exposure in the last 3 months	16 (80%)
PPI exposure in the last 3 months	11 (55%)
Treatment and Outcomes	
Antimicrobial usage	20 (100%)
Surgery or interventional radiology drainage	16 (80%)
ICU admission	11 (55%)
Mechanical ventilation	8 (40%)
Length of stay (days), median [IQR]	16 [11.25, 29.5]
Mortality	
30-day mortality	4 (20%)
90-day mortality	7 (35%)
Readmission	
30-day readmission	5 (25%)
90-day readmission	6 (30%)
Disposition	
Home	9 (45%)
Rehab facility	2 (10%)
Skilled nursing facility	3 (15%)
Hospice	3 (15%)
Died	3 (15%)

Results

A total of 20,594 samples from 13,139 patients were positive for CDI from any source. Among these, only 20 patients (0.15%) with EiCDI were identified. The mean age was 57.2 years and 55% were male. 50% of the samples were from abdominopelvic source while 25% were from either the blood or wound cultures. Fourteen patients (70%) were hospitalized within 12-weeks prior to their positive cultures and 80% were exposed to antibiotics within the prior 3 months. All patients had their infections treated with antibiotics and 16 (80%) underwent surgical intervention or drainage for source control. Eleven (55%) required admission to intensive care unit (ICU). Only 5 patients had concomitant CDI involving the colon or intestine. 20% of patients with EiCDI died within 30 days of diagnosis and 35% expired within 90 days. Readmissions were common with 25% and 30% at 30- and 90- days from discharge, respectively.

Conclusion

EiCDI is a rare event mostly seen as part of a polymicrobial infection and not frequently associated with intestinal CDI. This low frequency is likely a result of the anaerobic nature of this bacterium. Most patients with EiCDI required surgical intervention or drainage for source control and about half required high level of care including mechanical ventilation and/or ICU admission. EiCDI is associated with high rates of morbidity and mortality. Large prospective studies are needed to better understand optimal diagnosis and treatment this uncommon entity.