

Post-*Clostridioides difficile* Infection Irritable Bowel Syndrome: A Specialty Clinic Study



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BACKGROUND

- Clostridioides difficile* (*C. difficile*) is the most common cause of health care-associated infections in the U.S., contributing to significant morbidity and mortality among the elderly.¹⁻³
- Recurrence occurs in ~20-30% of patients.^{4,5} Recurrent CDI (rCDI) and post-infectious irritable bowel syndrome (PI-IBS) can be difficult to differentiate in clinical practice.
- Standard treatment for rCDI is antibiotics or fecal microbiota transplantation (FMT),¹ while treatment for IBS includes lifestyle or dietary modifications and symptomatic management.⁶ Conversely, treating PI-IBS with antibiotics can worsen gut dysbiosis and GI symptoms.^{8,9}
- Post-CDI IBS is a known sequela of CDI, but it is not as well-studied as PI-IBS secondary to other pathogens. Its prevalence has also not been well-established.

METHODS

- Study Description:** Retrospective study of unique patient encounters at the Complicated *C. difficile* clinic (CCDC) at the University of Virginia Health System.
- Data Collection:** Data retrospectively collected on patients seen from March 2020 to July 2021.
- Case Definition:**
 - CDI diagnosed if: (1) ≥ 3 liquid stools/day; (2) positive toxin (NAAT or enzyme immunoassay); (3) symptom improvement with antibiotics.
 - Post-CDI IBS diagnosed if: (1) persistent GI symptoms (BM irregularities, abdominal pain, discomfort, bloating, distention); (2) symptoms with specific triggers (food, stressors); (3) post-prandial diarrhea, bloating, or abdominal discomfort; (4) abdominal pain or relief with defecation; (5) temporal pattern. In addition, no other evidence for active infection (fever, leukocytosis, colitis by abdominal imaging); and no other causes of inflammatory intestinal conditions (enteric infections, IBD).
- Statistical Analysis:** SPSS software used. Analyses performed using Welch's t-tests, chi-squared tests, and Mann-Whitney U tests. Differences considered statistically significant when P value was < 0.05 .

Table 1. Characteristics of 67 Patients Referred to UVA Complicated *C. Difficile* Clinic

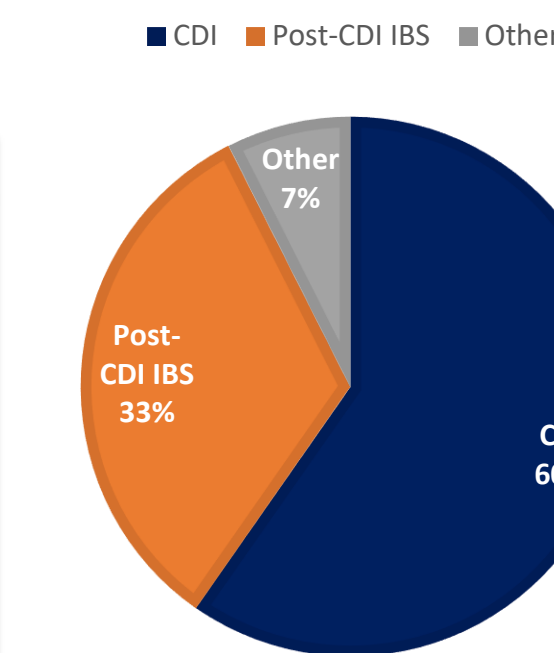
Variables	
Age mean (range)	64.2 (21-93)
Sex: female	51 (76.1%)
Race	
Black	2 (3.1%)
White	62 (95.4%)
Other	1 (1.5%)
Ethnicity	
Hispanic/Latin-American	1 (1.5%)
Comorbidities	
GI	
Crohn disease	2 (3.0%)
Ulcerative colitis	1 (1.5%)
Microscopic colitis	1 (1.5%)
IBS	5 (7.5%)
Psychiatric	
Depression	22 (32.8%)
Anxiety	15 (22.4%)
Neurologic	
Dementia	2 (3.0%)
Charlson Comorbidity Index mean (range)	3.8 (0-11)
Previous CDI episodes	
Treated CDI episodes mean (range)	3.0 (1-10)
Diagnosis	
CDI	40 (59.7%)
Recurrent CDI	32 (47.8%)
First episode of CDI	8 (11.9%)
Post-CDI IBS	22 (32.8%)
IBS-D	18 (26.9%)
IBS-C	1 (1.5%)
IBS-M	3 (4.5%)
Other diagnosis	5 (7.5%)

DISCLOSURES

There are no relevant financial disclosures.

RESULTS

CLINIC DIAGNOSIS



*Other: IBD, gastroenteritis, traveler's diarrhea, colonization

COMPARISON OF PATIENTS WITH CDI AND POST-CDI IBS

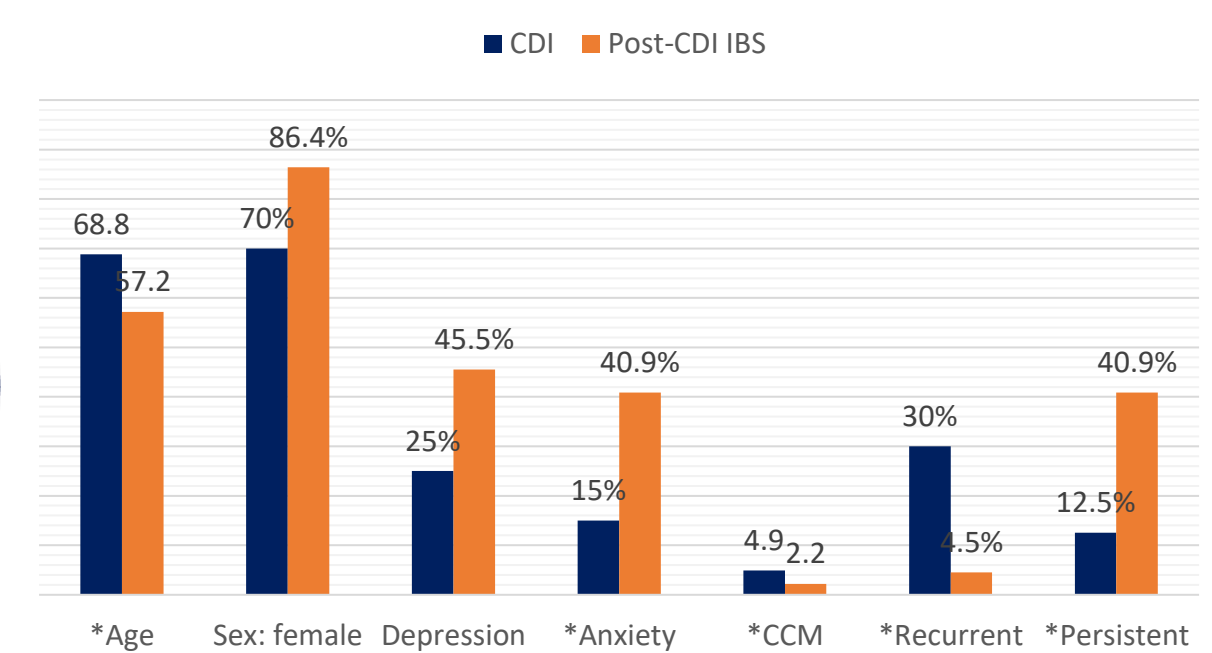


Table 2. Comparison between patients diagnosed with CDI and patients diagnosed with post-CDI IBS.

Variables	CDI (N = 40)	Post-CDI IBS (N = 22)	P-value
Age (mean)	68.8	57.2	0.03*
Sex: female	28 (70.0%)	19 (86.4%)	0.21
Comorbidities			
Depression	10 (25.0%)	10 (45.5%)	0.15
Anxiety	6 (15.0%)	9 (40.9%)	0.02*
Charlson Comorbidity Index (mean)	4.9	2.2	0.00006*
Previous CDI episodes			
Treated CDI episodes (mean)	3.2	2.7	0.25
3-months outcomes			
Recurrent CDI	12 (30.0%)	1 (4.5%)	0.02*
Recurrent diarrhea (non-CDI)	1 (2.5%)	3 (1.4%)	0.12
Persistent GI symptoms (non-CDI)	5 (12.5%)	9 (40.9%)	0.01*
Symptom resolution	13 (32.5%)	6 (27.3%)	0.77
FMT	5 (12.5%)	1 (4.5%)	0.40

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Table 3. Symptoms of post-CDI IBS patients at UVA Complicated *C. Difficile* Clinic

Symptoms	Number of post-CDI IBS patients with symptoms (n=22)
BM irregularities (inconsistent frequency and/or stool consistency; waxes and wanes).	22
Abdominal pain, discomfort, bloating, distention or hypersensitivity.	13
Symptoms occurring upon exposure to specific triggers (food or stress).	9
Post-prandial diarrhea, bloating, gaseousness or abdominal discomfort.	5
Abdominal pain or relief of pain with defecation.	2
Temporal pattern of loose bowel movement (occurring at specific period of the day, e.g. morning).	10

SUMMARY

- Out of 67 patients referred to the UVA CCDC, ~1/3 who were presumed to have rCDI actually exhibited symptoms of post-CDI IBS.
 - This percentage is similar to or higher than previously reported in the literature regarding post-CDI IBS (4-25%)¹⁰⁻¹³ and post-infectious IBS in general (10%)⁷.
- Post-CDI IBS was associated with younger age, history of anxiety, fewer medical comorbidities, and lower risk of recurrences than patients with CDI.
- Conclusion:** Important to ascertain diagnosis in patients with recurrent diarrhea and history of CDI to prevent unnecessary antibiotic treatment or interventions (FMT). While treatment for CDI is antibiotics, this could precipitate or exacerbate functional diarrhea or predispose to true recurrent CDI due to further alterations of gut microbiota.
- Limitations:** Small sample size and being a single-center study. Study period also overlapped with FMT via colonoscopy being on hold at medical centers using OpenBiome; therefore, there were patients with rCDI who would have benefited from FMT who did not receive it.