



Research Paper

Fecal Microbiota Transplantation in patients with Clostridioides Difficile Infection following COVID-19: A case series

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ABSTRACT

Introduction: During the COVID-19 pandemic, a marked increase in the incidence of Clostridioides Difficile Infection (CDI) was observed in Poland. This trend has been associated with widespread antibiotic use and healthcare burden during the SARS-CoV-2 pandemic. High disease severity, frequent recurrences, and limited therapeutic options continue to make CDI a significant clinical challenge.

Aim: To describe the clinical course and outcomes of Fecal Microbiota Transplantation (FMT) in patients with Clostridioides Difficile Infection following COVID-19.

Material and methods: This retrospective case series included four adult patients who developed CDI shortly after COVID-19. All patients underwent FMT between April and August 2021. Three patients experienced at least two severe recurrences before FMT, whereas one patient with fulminant CDI underwent FMT after the first episode. Clinical outcomes were assessed based on symptom resolution and absence of recurrence during follow-up.

Results and discussion: All patients experienced resolution of diarrhea and gastrointestinal symptoms following FMT. No CDI recurrences were observed during follow-up. No procedure-related complications were reported. Although limited by the small sample size, heterogeneous study population, and retrospective design, the findings suggest that FMT may be a feasible therapeutic option in selected patients with severe or recurrent CDI following COVID-19.

Conclusions: In this small retrospective case series, Fecal Microbiota Transplantation was associated with favorable clinical outcomes and absence of CDI recurrence during follow-up in patients with severe or recurrent CDI following COVID-19.

1. INTRODUCTION

The intestinal microbiota plays a crucial role in maintaining host health through its protective, trophic, and metabolic functions. Disruption of the intestinal microbiome during coronavirus disease 2019 (COVID-19) has been linked to multiple factors, including the enteric tropism of SARS-CoV-2, frequent antibiotic use, and gastrointestinal manifestations of the infection. Dysbiosis has been associated with an increased risk of sepsis, multiple organ failure, and hospital-acquired infections.¹ COVID-19 was associated with substantial morbidity and mortality, particularly among older adults, prompting extensive clinical research into its short- and long-term consequences.²

During the COVID-19 pandemic, the number of reported *Clostridioides Difficile* Infection (CDI) cases increased markedly in Poland. In 2021, 21,157 cases were reported, compared with 10,139 cases in 2020,³ representing more than a twofold increase. The increasing incidence of CDI posed a significant clinical challenge, particularly as infectious disease wards – and in some instances entire hospitals – were dedicated exclusively to patients with COVID-19. In the subsequent years (2022–2024), 21,563,⁴ 21,268,⁵ and 20,696⁶ cases were reported, respectively, indicating a persistently elevated burden of CDI requiring treatment.

Fecal Microbiota Transplantation (FMT), defined as the transfer of intestinal microorganisms from a healthy donor to a patient's gastrointestinal tract, has demonstrated remarkable efficacy, achieving cure rates of up to 90% in patients with recurrent CDI.^{7–9}

2. AIM

To describe the clinical outcomes and safety of Fecal Microbiota Transplantation (FMT) in patients with severe, recurrent, or fulminant *Clostridioides Difficile* Infection following COVID-19.

3. MATERIAL AND METHODS

This retrospective case series included four patients treated for severe, recurrent or fulminant *Clostridioides Difficile* Infection shortly after COVID-19. All patients had been hospitalized primarily due to COVID-19 pneumonia, and CDI developed shortly after hospital discharge.

CDI was diagnosed based on the presence of diarrhea (≥ 3 unformed stools within 24 hours) together with positive stool testing for toxigenic *Clostridioides Difficile* using a GDH/toxin assay, in accordance with institutional practice and contemporary guidelines. Endoscopic findings of pseudo-membranous colitis supported the diagnosis in severe cases.

Severe CDI was defined according to IDSA/SHEA criteria as used in institutional practice at the time of patient management, including leukocytosis $\geq 15 \times 10^9/L$ and/or serum creatinine > 1.5 mg/dL. Fulminant CDI was defined by hypotension, shock, ileus, or toxic megacolon.

All patients had received broad-spectrum antibiotic therapy during or shortly after COVID-19 hospitalization. Additional risk factors included advanced age, multiple comorbidities, and prolonged hospitalization.

All patients underwent FMT between April and August 2021 at the Regional Specialist Hospital in Olsztyn, Poland. Donor screening was performed in accordance with national regulations governing tissue and cell donation. During the COVID-19 pandemic, additional infectious safety measures were implemented, including epidemiological screening and SARS-CoV-2 RT-PCR testing of donors, in line with international safety recommendations for Fecal Microbiota Transplantation during the pandemic period.¹⁰

Clinical data were obtained from medical records and included demographic characteristics, comorbidities, clinical course of infection, treatment history, and outcomes following FMT.

All procedures were performed in accordance with institutional protocols, and written informed consent was obtained from all patients prior to FMT. Due to the retrospective nature of the study and use of routinely collected clinical data, formal approval from a bioethics committee was not required in accordance with local regulations.

4. RESULTS

We analyzed four patients – two men and two women – in their seventh and eighth decades of life (Table 1). A total of four Fecal Microbiota Transplantation procedures were performed between April and August 2021.

All patients presented with multimorbidity, defined as the presence of at least three chronic conditions, including chronic coronary syndrome, generalized atherosclerosis, paroxysmal atrial fibrillation, arterial hypertension, diabetes mellitus, pulmonary fibrosis with emphysema, and bronchial asthma.

Table 1. Clinical characteristics and treatment outcomes of patients undergoing Fecal Microbiota Transplantation.

Patient	COVID-19 (date)	First CDI episode (date)	CDI severity	Recurrences	Pre-FMT pharmacotherapy	CDI recurrence after FMT (Yes/No)
Male, 68 y	I 2021	IV 2021	Severe	2	Vancomycin, Fidaxomicin	No
Female, 74 y	III 2021	IV 2021	Severe	2	Vancomycin, Metronidazole, Rifaximin	No
Male, 71 y	IV 2021	V 2021	Fulminant	0	Vancomycin, Metronidazole	No
Female, 66 y	III 2021	IV 2021	Severe	3	Vancomycin, Fidaxomicin	No

Within a short period following COVID-19 infection, all patients developed severe or fulminant *Clostridioides Difficile* Infection, with endoscopic findings consistent with pseudomembranous colitis (Figure 1). Three patients experienced

at least two severe recurrences prior to Fecal Microbiota Transplantation despite receiving appropriate antibiotic therapy and adhering to recommended hygiene measures in the home environment. In one patient, rifaximin was administered as

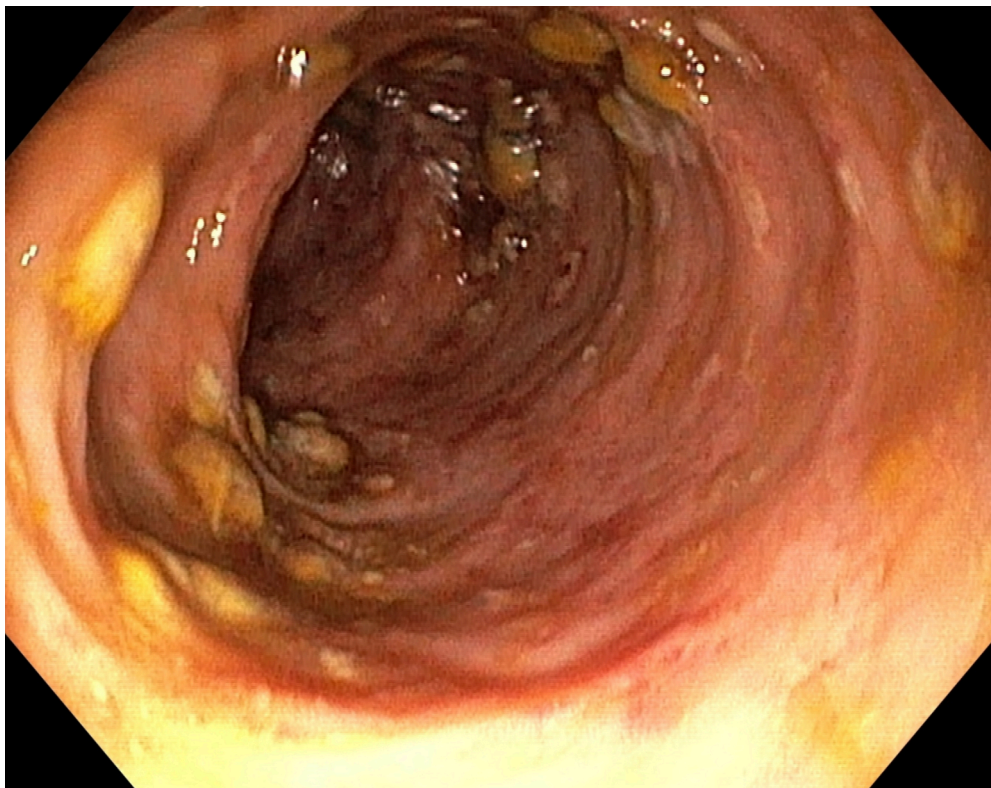


Figure 1. Colon with pseudomembranous colitis visible during colonoscopy.

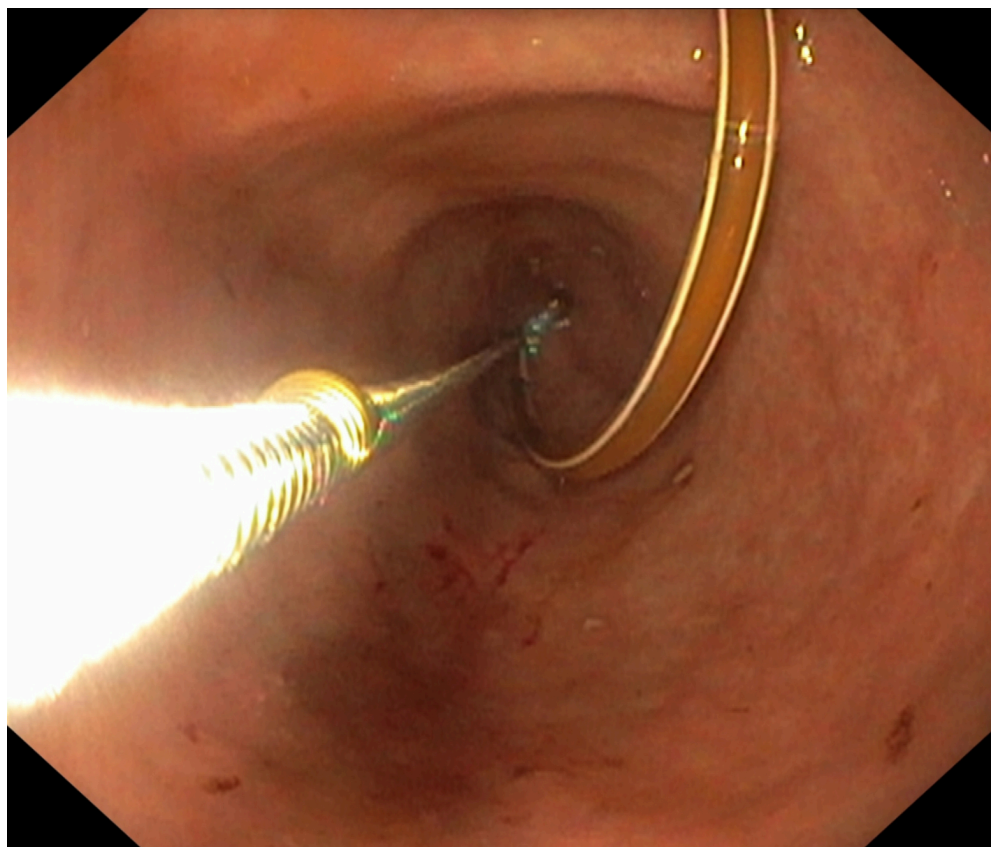


Figure 2. Placement of a nasoduodenal tube through the pylorus into the duodenum using forceps.

a post-vancomycin “chaser” therapy in the setting of multiple CDI recurrences prior to Fecal Microbiota Transplantation (FMT). One patient, due to the fulminant course of infection, underwent FMT after the first episode of CDI.

FMT was performed following bowel preparation with macrogol. A nasoduodenal tube was inserted and positioned in the distal duodenum under endoscopic guidance (Figure 2). The microbiota preparation was administered through the tube without retrograde flow into the stomach. All procedures were completed without complications, and patients were discharged on the same day. Gastroscopy was selected as the delivery route due to severe colonic inflammation associated with CDI, which increased the procedural risk of colonoscopy.

During follow-up ranging from 3 to 6 months, all patients achieved complete resolution of gastrointestinal symptoms. No recurrences of CDI were observed.

5. DISCUSSION

Fecal Microbiota Transplantation (FMT) is an increasingly used therapeutic approach in Poland, with the first successful procedure performed in 2012.⁸ Its high efficacy in recurrent *Clostridioides Difficile* Infection (CDI), reaching approximately 90%, and durable clinical response make FMT an important treatment option, particularly in the context of the persistently high burden of CDI observed during and after the COVID-19 pandemic.^{7,8} Additional benefits include reduced antibiotic exposure, a potential decrease in antimicrobial resistance burden, shorter hospitalization, and reduced risk of hospital-acquired infections.^{8,11,12}

Current international guidelines support a structured approach to CDI management. According to the 2021 IDSA/SHEA focused update, fidaxomicin and vancomycin remain first-line therapies, while FMT is recommended in patients with multiple recurrences after failure of appropriate antimicrobial treatment.¹³ Similarly, the ESCMID guideline emphasizes fidaxomicin or vancomycin as standard initial therapy, with FMT reserved for recurrent CDI or selected difficult-to-treat cases.¹⁴ The 2024 American Gastroenterological Association (AGA) guideline on microbiome-based therapies further supports FMT as an effective intervention for recurrent CDI, while highlighting its favorable benefit – risk profile in appropriately selected patients. The guideline also discusses bezlotoxumab as an adjunctive therapy for the prevention of recurrence in high-risk patients;¹⁵ however, its availability remains limited in some settings, including Poland. In selected severe cases, earlier use of FMT may be considered when disease is fulminant or refractory. In our cohort, one patient underwent FMT after the first episode of fulminant CDI due to high-risk clinical presentation, achieving sustained remission without recurrence.

The intestinal microbiota plays a key role in systemic immune regulation, and its disruption has been implicated in infectious disease susceptibility. The gut-lung axis describes bidirectional interactions between the intestinal and respiratory microbiota mediated by microbial metabolites and

immune pathways.^{7,16} Viral infections, including SARS-CoV-2, may induce gut dysbiosis, while microbiome alterations may influence systemic immune responses and disease susceptibility.^{1,7,16} Although modulation of the gut microbiota through FMT has been hypothesized to influence the clinical course of COVID-19, this was not evaluated in the present study, which focused exclusively on CDI outcomes in patients with prior SARS-CoV-2 infection.^{16,17}

During the COVID-19 pandemic, Fecal Microbiota Transplantation programs implemented additional donor safety screening due to concerns regarding potential SARS-CoV-2 transmission.^{7,9,11}

Safety remains an important consideration in FMT practice. Available evidence suggests a favorable safety profile. Randomized trials and observational studies have demonstrated high efficacy of FMT compared with standard antibiotic therapy in recurrent CDI, with adverse events generally being mild and self-limiting.^{18,19} According to the 2024 AGA guideline, FMT is considered a safe and effective microbiome-based therapy in appropriately selected patients.¹⁵ No serious procedure-related adverse events were observed in our cohort.

Modulation of the intestinal microbiota may also be considered as a preventive strategy in patients at increased risk of CDI. Although current evidence does not support routine probiotic use for CDI prevention, preliminary data suggest potential benefits in selected populations. In a pilot randomized study of hospitalized patients in coma, supplementation with *Bifidobacterium animalis* and *Bifidobacterium breve* was associated with a significant reduction in stool *Clostridioides Difficile* concentration;²⁰ however, these findings should be interpreted cautiously due to the small sample size and the use of microbiological rather than clinical outcomes.

This study has several limitations. It is a small retrospective case series with a heterogeneous patient population, lacking a control group and with limited follow-up duration. Moreover, the observational design precludes conclusions regarding causal relationships between prior COVID-19, CDI severity and treatment response.

6. CONCLUSIONS

In this small retrospective case series, Fecal Microbiota Transplantation was associated with favorable clinical outcomes and sustained remission without CDI recurrence during short-term follow-up in patients with severe or recurrent CDI following COVID-19.

Ethics approval

This retrospective case series was based on the analysis of anonymized clinical data collected during routine medical care. According to institutional regulations, approval from an Ethics Committee was not required. All procedures performed were in accordance with the ethical standards of the institution and with the Declaration of Helsinki.

Informed consent

The study was retrospective and involved the analysis of data obtained during routine clinical practice. Separate informed consent for participation in the study was not required. Patients provided informed consent for the diagnostic and therapeutic procedures performed as part of standard medical care.

Conflict of interest

None declared.

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None declared.

Author contributions

Study design: TA

Data collection: AB-F, AB-W

Statistical analysis: AB-F

Data interpretation: AB-F, AB-W, TA

Manuscript preparation: AB-F, AB-W

Literature search: AB-F, AB-W

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