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Original Article

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Clinical Approaches to *Clostridioides difficile* Infection Management: Insights From a Nationwide Survey of Korean Physicians

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ABSTRACT

Background: *Clostridioides difficile* infection (CDI) remains a significant public health challenge, with variable diagnostic and treatment practices. This study evaluated current clinical practices for CDI diagnosis and management in Korean physicians through a nationwide survey.
Methods: An online survey was conducted among physicians treating CDI, including gastroenterologists and infectious disease specialists. The survey covered diagnostic approaches, treatment regimens, and management strategies, including differentiation based on disease severity and recurrence.
Results: A total of 300 physicians responded. The most commonly reported indication for CDI testing was the occurrence of three or more diarrheal episodes within a 24-hour period. The majority of physicians (69.7%) preferred multiple diagnostic tests, favoring

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simultaneous testing (90.4%) over a stepwise approach. Preferred tests included nucleic acid amplification test (NAAT) (69%), glutamate dehydrogenase+toxin A/B combined assay (56%) and toxin enzyme immunoassay (EIA) (48%). Single-test users preferred toxin EIA (37.4%) and NAAT (29.7%). Treatment was primarily tailored to severity by 84.1% of physicians. For non-severe CDI, oral vancomycin (50.7%) and metronidazole (29%) were the main treatments, with 88% not recommending hospitalization. Severe CDI was treated with oral vancomycin (45.3%) or intravenous metronidazole in combination (44.9%), often for ≥ 14 days. For the first recurrence, 69.3% used oral vancomycin, with 22.6% opting for a tapered/pulsed regimen. Fecal microbiota transplantation use increased from 0.3% initially to 17.6% for multiple recurrences. In CDI with ileus, 64% preferred combination therapy, and 48% used vancomycin enemas. In inflammatory bowel disease patients, 99% underwent CDI testing for worsening diarrhea. Immunomodulators and biologics were continued in 79% and 73% of non-severe cases, respectively, but often paused during severe CDI.

Conclusion: Korean physicians generally follow the recently developed Korean guideline for CDI practice, but certain gaps and inconsistencies in choices were observed in clinical situations. Further efforts are needed to monitor guideline implementation and to analyze gaps between guideline recommendations and real-world clinical practice to optimize CDI management in Korea.

Keywords: *Clostridioides difficile* Infection; CDI Diagnosis; CDI Treatment; Recurrent CDI

INTRODUCTION

Clostridioides difficile infection (CDI) is a leading cause of healthcare-associated infectious diarrhea and a growing public health concern worldwide. Over the past two decades, the global incidence, severity, and mortality rates of CDI have risen significantly.[1,2] This sharp increase highlights CDI as a critical clinical and epidemiological challenge that demands targeted management strategies, prompting the publication of several guidelines incorporating the latest research data.

In Korea, the incidence of CDI has also steadily increased from 2008 to 2020, approaching levels observed in western countries.[3,4] This upward trend is likely driven by increased antibiotic use, an aging population, and the expanded healthcare services, factors expected to further exacerbate the incidence and severity of CDI in the future.[5] Despite these epidemiological shifts, inconsistencies in diagnostic and treatment practices persist across medical institutions in Korea, with many physicians relying on western guidelines that do not fully account for the clinical characteristics of CDI in Korea and the realities of the local healthcare environment.[6-8]

Significant variability in CDI diagnostic practices exists across medical institutions in Korea, emphasizing the urgent need for a standardized diagnostic protocol.[9] Although various diagnostic methods are available, inadequate management of specimen conditions is frequently reported.[9] Additionally, distinguishing asymptomatic carriers from true CDI cases remains a diagnostic challenge.[10]

Moreover, major obstacles in directly adopting western guidelines for CDI treatment in Korea are the limited availability of certain therapeutic agents and the regional and national differences in the CDI strain epidemiology.[11] These differences significantly

influence therapeutic choices across countries. For instance, while recent international guidelines recommend fidaxomicin as the first-line treatment for CDI,[6] its high cost and limited accessibility in Korea have led to the predominant use of more practical alternatives such as metronidazole and vancomycin.[12] The recently published Korean guideline for CDI (December 2024) has addressed many of these issues, yet some challenges remain in applying these recommendations to the diverse clinical settings.[13]

Therefore, this study aimed to assess the current clinical practices of Korean physicians regarding the diagnosis and treatment of CDI through a nationwide survey. The survey was conducted prior to the publication of the Korean clinical practice guidelines in December 2024, and its findings were utilized as foundational data to inform the development of these guidelines, reflecting the domestic clinical context. By systematically organizing and analyzing the survey results, this study also aims to provide a basis for future research to evaluate the implementation of the newly developed guidelines and to address the gaps between guideline recommendations and real-world clinical practice.

METHODS

Survey

A cross-sectional, voluntary online survey was conducted between January and February 2024. The survey was administered using the secure SurveyMonkey platform (https://www.surveymonkey.com). Participants accessed the questionnaires through email-distributed links hosted on the platform. To ensure anonymity, no personally identifiable information was collected. All survey data were stored in a password-protected database. Email invitations to participate were sent three times to members of the Korean Association for the Study of Intestinal Diseases (KASID) and the Korean Society of Infectious Diseases (KSID). The survey was distributed via email to approximately 800 members of the KASID of whom 208 responded (response rate: ~26%). In addition, the survey was conducted among executive and committee-level members of the KSID. As participation was voluntary, selection bias may have occurred.

The survey, conducted in Korean, aimed to assess physicians' perspectives on CDI management strategies. It consisted of eight key domains: respondent characteristics, diagnosis, treatment of non-severe CDI, treatment of severe CDI, treatment of recurrent CDI, fecal microbiota transplantation (FMT) in CDI, CDI in special situations such as CDI with concurrent ileus and CDI in patients with inflammatory bowel disease (IBD). A 'stepwise' diagnostic algorithm was defined as the sequential application of two or more diagnostic tests for CDI. For selected questions, respondents were allowed to select multiple responses, particularly for treatment strategies in specific clinical scenarios such as CDI with ileus.

Before distribution, the survey underwent expert review, validation, and refinement to ensure clarity, relevance, and appropriateness. An English version of the detailed questionnaire is provided in **Supplementary Data 1** for reference.

Statistical analysis

Categorical variables were presented as frequencies and percentages, while continuous variables were expressed as means ± standard deviations. All statistical analyses were conducted using R Studio version 4.3.1 (2023) (RStudio, Boston, MA, USA).

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For subgroup analysis, respondents were stratified by age 50, as this threshold is considered clinically meaningful for comparing mid-career and senior physicians. Among all respondents, 23.7% (n = 71) were aged 50 or older.

Ethics statement

This study was approved by the Institutional Review Board (IRB) of the Chung-Ang University Gwangmyeong Hospital (IRB No. 2401-134-006). Informed consent was waived by the board.

RESULTS

Demographics of the respondents

Among the 300 physicians who participated (**Table 1**), the majority were employed at tertiary hospitals (57.0%, n = 171), followed by secondary hospitals (35.7%, n = 107) and primary clinics (7.0%, n = 21). Gastroenterologists accounted for 52.3% (n = 157) and infectious disease specialists comprised 29.3% (n = 88).

Patterns in CDI diagnosis

The majority of physicians (90.3%, n = 271) reported initiating CDI diagnostic testing for hospitalized patients presenting with diarrhea (Bristol stool forms 6–7), with most (47.7%) testing after three or more episodes of abnormal stools within a 24-hour period.

Table 1. Demographics of the respondents

Variables	Total (N = 300)
Age, yr	43.68 ± 7.65
< 50	229 (76.3)
≥ 50	71 (23.7)
Sex	
Male	183 (61.0)
Female	117 (39.0)
Years of clinical practice	
< 5	78 (26.0)
5–9	61 (20.3)
10–14	69 (23.0)
≥ 15	92 (31.7)
Practice setting	
Primary care clinic	21 (7.0)
Community hospital	107 (35.7)
University hospital	171 (57.0)
Specialized diagnostic laboratory	1 (0.3)
Specialty	
Gastroenterologist	157 (52.3)
Infectious disease specialists	88 (29.3)
Internal medicine (other than above mentioned)	15 (5.0)
Pediatrician	
Infectious disease specialists	4 (1.3)
Gastroenterologist	6 (2.0)
Others	6 (2.0)
General surgery	8 (2.7)
Laboratory medicine	8 (2.7)
Family medicine	3 (1.0)
General practitioner	3 (1.0)
Others[a]	2 (0.7)

Values are presented as mean ± standard deviation or number (%).
[a]Cardiothoracic surgeon and emergency physician.

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Table 2. Real-world practice for *Clostridioides difficile* infection diagnosis among Korean physicians

Characteristics	Values
Single test	91 (30.3)
Toxin EIA	34 (37.4)
GDH+toxin combined assay	20 (22.0)
NAAT	27 (29.7)
Culture	5 (5.5)
Multiple tests	209 (69.7)
Simultaneous testing	189 (90.4)
Toxin EIA	101 (48.0)
GDH+toxin A/B combined	118 (56.0)
NAAT	144 (69.0)
Culture	59 (28.0)
Stepwise approach	20 (9.6)
Toxin EIA	2 (10.0)
GDH	2 (10.0)
GDH+toxin combined	12 (60.0)
NAAT	4 (20.0)

Values are presented as number (%). Only the four most frequently used testing tools are presented.
EIA = enzyme immunoassay, GDH = glutamate dehydrogenase, NAAT = nucleic acid amplification test.

Diagnostic methods varied. While 30.3% (n = 91) used a single-test approach, the majority (69.7%, n = 209) adopted multiple-test strategies (**Table 2**). Among single-test users, nucleic acid amplification tests (NAAT, 29.7%), toxin A/B enzyme immunoassays (toxin EIA, 37.4%), and glutamate dehydrogenase (GDH)+toxin combined assays (22.0%) were the most common. For multiple-test users, nearly all (90.4%, 189) physicians preferred simultaneous testing with NAAT (69.0%) and GDH+toxin assays (56.0%) being predominant. Although rare, respondents who preferred stepwise algorithms (9.6%) typically started with GDH+toxin combination assays (60.0%), followed by NAAT (20.0%).

Subgroup analysis revealed that physicians in tertiary care hospitals predominantly employed multiple-test strategies (81.3%, n = 139), with a strong preference for simultaneous testing (90.6%, n = 126). In contrast, physicians in secondary care hospitals and primary care clinics reported greater reliance on single-tests approaches (45.2%, n = 57), likely reflecting resource limitations.

Regarding endoscopic practices, 33.3% (n = 100) indicated that they selectively use endoscopy to assess CDI severity rather than for primary diagnosis, while 28% (n = 84) reported reserving endoscopy for cases where non-invasive stool tests yielded inconclusive results.

Differentiation of treatment for severe and non-severe CDI

In treatment practices, 84.1% (n=249) tailored therapy based on disease severity. Most respondents (88.1%, n = 214) did not recommend hospitalization for newly diagnosed non-severe CDI.

Selection of treatment strategies for non-severe and severe CDI

For non-severe CDI (**Table 3**), oral vancomycin (50.7%) and oral metronidazole (29.0%) were the most commonly selected first-line regimens. Among respondents, the most commonly used vancomycin regimen was 125 mg four times daily for 10–13 days, whereas metronidazole was typically prescribed at 500 mg three times daily (**Supplementary Table 1**). Subgroup analysis by healthcare settings revealed that while 41.6% of respondents in primary and secondary care facilities preferred metronidazole, only 29.9% from tertiary hospitals prescribed metronidazole.

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Table 3. Survey results of opinions on the first-line treatment for non-severe *Clostridioides difficile* infection

Characteristics	Regimen	Values
Oral metronidazole		86 (29.0)
Dosage[a]	500 mg tid	68 (79.1)
	250 mg tid	10 (11.6)
Oral vancomycin		149 (50.7)
Dosage[a]	125 mg qid	129 (86.6)
	250 mg qid	11 (7.4)
Combination (oral vancomycin + IV metronidazole)		5 (1.7)
IV metronidazole		7 (2.3)

Values are presented as number (%).
[a]The two most frequent responses are presented.

Table 4. Survey results of opinions on the first-line treatment for severe *Clostridioides difficile* infection

Characteristics	Regimen	Values
Oral metronidazole		17 (7.0)
Dosage[a]	500 mg tid	12 (70.6)
	250 mg tid	2 (11.8)
Oral vancomycin		110 (45.3)
Dosage[a]	125 mg qid	72 (65.5)
	250 mg qid	25 (22.7)
	500 mg qid	8 (7.3)
Combination (oral vancomycin + IV metronidazole)		109 (44.9)
IV metronidazole		7 (2.9)

Values are presented as number (%).
[a]Two or three most frequent answer choices presented.

For severe CDI (**Table 4**), physicians favored oral vancomycin alone (45.3%) or combination therapy with oral vancomycin and intravenous (IV) metronidazole (44.9%). The most prescribed vancomycin regimen was 125 mg 4 times daily (65.5%), with 56.9% preferring a treatment duration of 10–13 days (**Supplementary Table 1**). Subgroup analysis by age (< 50 vs. ≥ 50 years) revealed notable differences. Respondents aged ≥ 50 years were more likely to prescribe metronidazole as a first-line treatment compared to those under 50 years particularly for non-severe CDI (43.9% vs. 32.1%) (**Supplementary Table 2**).

Selection of treatment strategies for recurrent CDI

For recurrent CDI (**Table 5**), most respondents preferred oral vancomycin (69.3% for first recurrence; 45.7% for ≥ 2 recurrences) with an increased use of tapered or pulsed regimens

Table 5. Survey results of opinions on the treatment for recurrent *Clostridioides difficile* infection

Characteristics	Regimen	1st recur	2nd or more recur
Oral metronidazole		33 (11.5)	9 (3.2)
Dosage[a]	500 mg tid	26 (78.8)	6 (66.7)
	250 mg tid	3 (9.1)	3 (33.3)
Oral vancomycin		199 (69.3)	129 (45.7)
Dosage[a]	125 mg qid	98 (49.2)	21 (16.3)
	125 mg qid (tapered/pulsed)	45 (22.6)	54 (41.9)
	250 mg qid	38 (19.1)	29 (22.5)
	500 mg qid	6 (3.0)	6 (4.7)
	500 mg qid (tapered/pulsed)	6 (3.0)	12 (9.3)
Combination (oral vancomycin + IV metronidazole)		49 (17.1)	95 (33.7)
IV metronidazole		5 (1.7)	4 (1.4)
FMT		1 (0.3)	45 (16.0)

Values are presented as number (%).
IV = intravenous, FMT = fecal microbiota transplantation.
[a]Only the most frequently selected dosage regimens are presented: the top 2 for oral metronidazole and the top 5 for oral vancomycin.

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for multiple recurrences (**Supplementary Table 3**). Notably, FMT was rarely selected for a first recurrence (0.3%) but considered by 16.0% for multiple recurrences. Subgroup analysis by age revealed that respondents aged ≥ 50 years were more likely to prescribe metronidazole than their younger counterparts, both for the first recurrence (16.2% vs. 10.0%) and for second or subsequent recurrences (6.0% vs. 2.3%) (**Supplementary Table 4**).

CDI with ileus

In CDI with ileus, respondents were asked to select preferred treatment strategies. Combination therapy with oral vancomycin and intravenous metronidazole was selected by 64% of respondents, while 23% reported using intravenous metronidazole alone and 48% reported using vancomycin enemas. As multiple responses were allowed, percentages may exceed 100%.

FMT in CDI

FMT is still infrequently performed in most clinical settings as approximately 59.9% of respondents indicated having performed FMT, with the majority (69.4%) reporting limited experience (< 5 cases). The most common indications for FMT included severe CDI at initial diagnosis (16.2%) and ≥ 2 recurrences (89.2%).

Treatment strategies for CDI in patients with IBD

We solicited additional inquiries regarding CDI in IBD from gastroenterologists who treat IBD patients. Among 141 physicians who responded, 99% performed CDI testing in patients with IBD experiencing diarrhea exacerbation. The most reported regimen was oral vancomycin (66%), 125 mg four times daily (79.6%) for 7–14 days (98.9%). However, 25% still prescribed oral metronidazole. For IBD patients with non-severe CDI, the majority continued using immunomodulators (79.4%, n = 104) and biologics (73.3%, n = 96). In contrast, for managing severe CDI, they often discontinued immunomodulators (67.2%, n = 88) and biologics (67.9%, n = 89).

Surgical management for severe or fulminant CDI

In cases where severe or fulminant CDI did not respond promptly to treatment, 20.6% (n = 57) would consider surgical intervention. Colectomy (n = 34, 59.6%) was the most preferred procedure, followed by ileostomy with additional lavage (n = 22, 38.6%).

Comparison between gastroenterologists and infectious disease specialists

While both specialties predominantly followed guideline-based approaches, gastroenterologists were more likely to perform endoscopic evaluation, repeat diagnostic testing for false negatives, and follow-up testing after treatment, indicating a stronger emphasis on direct visualization and reassessment (**Table 6**). Gastroenterologists reported greater experience with FMT and were more likely to refer patients to specialized centers for treatment. Despite differences in diagnostic and procedural preferences between the two specialties, both groups demonstrated similar patterns in therapeutic choices across the treatment spectrum from non-severe to recurrent CDI, indicating a shared approach to CDI management and providing a strong basis for multidisciplinary collaboration.

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Table 6. Subgroup analysis in CDI management between gastroenterologists and infectious disease specialist

Survey item	Gastroenterologists	Infectious disease specialists
Diagnosis		
Multiple tests	112 (71.3)	64 (72.7)
Perform endoscopy		
Always	16 (10.3)	0 (0.0)
Generally, do not perform	20 (12.8)	42 (48.3)
Generally, do not perform, but cases for severity check	63 (40.4)	20 (23.0)
Only when clinically suspicious but lab tests are negative	55 (35.3)	24 (27.6)
Repeat test		
Usually (≥ 80%) do not perform when clinically suspicious (considering of false negative)	48 (30.8)	46 (52.9)
	103 (66.0)	39 (44.8)
Follow-up test		
After treatment	24 (15.4)	3 (3.4)
Treatment		
Non-severe CDI		
Oral metronidazole	38 (29.5)	25 (30.9)
Oral vancomycin	86 (66.7)	52 (64.2)
Severe CDI		
Oral metronidazole	15 (9.7)	3 (3.4)
Oral vancomycin	72 (46.8)	48 (55.2)
Oral vancomycin + IV metronidazole	62 (40.3)	36 (41.4)
Medically refractory CDI		
Surgical intervention	30 (19.9)	22 (26.5)
Vancomycin enema in severe CDI	33 (24.1)	32 (36.8)
1st recurred CDI		
Oral metronidazole	7 (8.1)	16 (10.4)
Oral vancomycin	110 (71.4)	72 (83.7)
Oral vancomycin + IV metronidazole	26 (16.9)	7 (8.1)
≥ 2nd recurrent CDI		
Oral vancomycin	68 (45.0)	47 (54.7)
Oral vancomycin + IV metronidazole	46 (30.5)	26 (30.2)
FMT	32 (21.2)	11 (12.8)
FMT		
Experienced	74 (49.0)	32 (38.6)
Consider		
Referral to higher institution to perform FMT	41 (27.2)	16 (19.3)

Values are presented as number (%).
CDI = *Clostridioides difficile* infection, IV = intravenous, FMT = fecal microbiota transplantation.

DISCUSSION

The diagnosis and management of CDI in Korea remain heterogeneous, with ongoing challenges in standardizing diagnostic methods and optimizing treatment strategies. Previous studies have highlighted inconsistencies in diagnostic approaches, rising CDI incidence, and variability in treatment selection, all of which align with the findings of our nationwide survey.[3,14,15] This survey aimed to comprehensively assess the current practices among Korean physicians in the diagnosis and treatment of CDI.

C. *difficile* strains exhibit distinct regional distribution patterns, with notable differences in strain types, characteristics, and antibiotic resistance profiles. The epidemiology of CDI strains in Asia differs from that in western countries.[16] While the hypervirulent ribotype 027 (RT027) strain has been a major concern in North America and Europe, it has been rarely reported in Korea and other Asian regions.[12,14,17] Instead, studies have shown that toxin A-negative, toxin B-positive (tcdA−/tcdB+) strains are prevalent in Korea, accounting for up to 27% of toxigenic strains.[12,17] Therefore, implementing cost-effective and resource-efficient

treatment strategies that account for the unique features of *C. difficile* strains in Korea is essential for optimizing patient outcomes and ensuring effective resource allocation.

The incidence of CDI in Korea has been steadily increasing, as demonstrated by both active surveillance and national healthcare data. Kim et al.[3] conducted a prospective multicenter study, reporting a CDI incidence of 7.04 per 10,000 patient-days and 4.69 per 1,000 admissions, rates comparable to those in the United States and Europe. Furthermore, an analysis of Health Insurance Review and Assessment Service (HIRA) data (2008–2020) showed a significant rise in CDI cases across all hospital settings. Notably, the incidence of CDI was higher in general hospitals than in tertiary hospitals in the active surveillance compared to HIRA-reported data. This discrepancy may be attributed to differences in infection control measures and diagnostic testing accessibility between secondary and tertiary hospitals, particularly the implementation of active surveillance for diarrheal patients in some institutions. These findings align with our study, suggesting that CDI remains underdiagnosed, particularly in non-tertiary settings. Tertiary hospitals typically have greater access to diagnostic resources and medications, facilitating guideline-concordant practices with stepwise testing and vancomycin-based regimens. In contrast, secondary and primary care institutions may face resource limitations, which may partially explain the reliance on single-test diagnostic methods and metronidazole therapy. These results emphasize the importance of enhanced surveillance and awareness strategies as well as targeted educational interventions and resource allocation to improve CDI detection and evidence-based CDI management in all healthcare settings in Korea.

In terms of diagnostic methods, a systematic review and meta-analysis conducted by Korean researchers using domestic data emphasized that although GDH EIAs and NAATs demonstrate high sensitivity, toxin A/B EIAs alone are inadequate for reliable CDI diagnosis. Meanwhile, GDH EIAs are limited by their low specificity, as they detect both toxigenic and non-toxigenic strains, and NAATs, despite their diagnostic accuracy, may lead to overdiagnosis of asymptomatic carriage and entail high costs and technical demands.[18] In line with our study, a nationwide survey of clinical laboratories in Korea found that 73% of institutions employed multiple diagnostic methods, with toxin A/B EIAs (84.3%) and NAATs (58.4%) being the most commonly used components.[15] Another recent Korean study reported that only half of participating hospitals had access to GDH testing.[3]

The finding that most physicians preferred using two or more diagnostic tests supports the need for a stepwise diagnostic algorithm to improve the accuracy in CDI detection. A figure illustrating the recommended diagnostic algorithm according to the recently developed Korean guideline is provided in **Supplementary Fig. 1**.[13] However, approximately 37% of respondents, a considerable proportion, reported using toxin A/B EIAs alone, which may compromise diagnostic accuracy due to their low sensitivity and highlights the need for corrective measures. Diagnostic approaches also varied by type of healthcare institution. While tertiary hospitals predominantly adopted multi-testing strategies, secondary and primary care institutions were more likely to rely on single-test methods—likely reflecting differences in resource availability and diagnostic infrastructure. Notably, the continued presence of such infrastructural limitations in general hospitals, where CDI incidence tends to be higher, suggests that limited test availability, challenges in appropriate patient selection, and insufficient disease awareness may contribute to underdiagnosis.[3] Furthermore, the relatively low adoption rate of NAATs in Korea compared to international guidelines underscores the need for further discussion and consideration regarding the broader implementation of NAATs in clinical practice.

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Regarding treatment strategies, oral vancomycin was the most frequently prescribed first-line therapy for both initial episodes of non-severe and severe CDI. This finding aligns with western guidelines, which advocate for oral vancomycin or fidaxomicin as the first-line treatment for CDI, regardless of disease severity. In contrast, earlier nationwide data from Korea indicated that oral metronidazole was previously the most used first-line therapy (61.9%).[4] While there has been a shift toward oral vancomycin, a substantial proportion of physicians, particularly those in primary care settings and physicians aged ≥ 50, continued to prescribe metronidazole, citing its cost-effectiveness and accessibility. This trend was particularly pronounced among physicians aged ≥ 50. Older physicians may be more accustomed to traditional practices, such as the use of metronidazole as first-line therapy. However, considering the differences in CDI strains and antibiotic susceptibility patterns between Korea and western countries, treatment strategies should be adapted accordingly. It remains unclear whether these epidemiological factors influence physicians' antibiotic selection.

Interestingly, current Japanese and Taiwanese guidelines[19,20] still recommend oral metronidazole as the preferred treatment for an initial episode of non-severe CDI. This discrepancy among clinical guidelines may be attributed to differences in the prevalence of hypervirulent CDI strains, such as BI/NAP1/027. Compared to the United States, where this strain is more prevalent,[21] Asian countries have so far reported relatively lower or negligible incidence rates.[12,14,17] Given these findings, further randomized controlled trials reflecting real-world clinical practice in Korea are necessary to establish clear evidence regarding the cost-effectiveness and long-term outcomes of different treatment options, particularly for patients with an initial episode of non-severe to moderate CDI.

This survey revealed that a significant proportion of physicians preferred combination therapy with oral vancomycin and IV metronidazole, as well as adjunctive vancomycin enema, for severe CDI and CDI with ileus. In such cases, IV metronidazole or vancomycin enema is used to achieve therapeutic concentrations when gastrointestinal transit may be compromised, although high-quality evidence remains limited. However, recommendations regarding these approaches differ across guidelines. The IDSA, ACG, Taiwan, and Poland guidelines suggest that IV metronidazole and/or vancomycin enema may be considered in fulminant CDI with ileus, acknowledging the limited evidence supporting these adjunctive treatments.[2,6,7,20,22] In contrast, the European guidelines do not recommend routine combination therapy,[8] and the Japanese guidelines advise adding metronidazole only if oral vancomycin is ineffective.[19] The recent Korean guidelines conditionally recommend the combination of oral vancomycin and IV metronidazole with adjunctive vancomycin enema for CDI with ileus, although the level of evidence is very low.[13] In our survey, approximately half of the respondents reported using combination therapy with additional vancomycin enema in CDI patients with ileus, reflecting these international trends and current guideline suggestions.

The management of recurrent CDI showed distinct trends, with an increased reliance on tapered or pulsed vancomycin regimens and greater consideration of FMT for multiple recurrences. Despite its growing role, FMT remains underutilized. Our study aligns with the findings from Kim et al.,[3] which demonstrated low referral rates to specialized institutions for FMT, despite increasing evidence supporting its efficacy in recurrent CDI. Subgroup analysis revealed disparities in FMT adoption based on healthcare setting, physician subspecialty, and age, with younger physicians (< 50 years) more likely to incorporate FMT into their treatment approach. The barriers to FMT implementation in Korea likely stem from regulatory constraints, limited availability, and physicians' experience. To increase

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its use in refractory CDI cases, expanding access to FMT and establishing clear national guidelines will be essential.

In IBD patients, although the majority of physicians prescribed oral vancomycin as the first-line treatment for CDI, a substantial proportion (25%) continued to use oral metronidazole. To date, no RCTs have directly compared oral metronidazole and oral vancomycin in this patient population, and the available evidence remains limited. However, observational studies have suggested that oral metronidazole monotherapy in IBD patients with CDI may be associated with higher hospitalization rates, longer hospital stays, and increased recurrence rates.[23,24] CDI in IBD patients has been associated with an increased risk of disease exacerbation and a higher recurrence rate compared to the general population. Both the ACG and ECCO guidelines recommend oral vancomycin or fidaxomicin as the preferred treatment options for CDI in patients with IBD.[7,25] However, fidaxomicin is not currently available in Korea. Accordingly, the most recent Korean guidelines recommend oral vancomycin as the first-line therapy for IBD patients with CDI, but this is a conditional recommendation based on very low-quality evidence, reflecting limitations in both the evidence base and the availability of treatment options.

Despite the recent establishment of Korean clinical guideline for CDI, certain challenges remain unaddressed in real-world practice. Key gaps include limited access to recommended diagnostic tools in the primary and secondary hospitals and barriers to FMT implementation. To address these gaps, we should focus on the enhanced dissemination and education on the updated guidelines and strategic allocation of resources to expand diagnostic and therapeutic options possibly along with nationwide antimicrobial stewardship demonstration project.

A key strength of this study is the inclusion of a meaningful number of physicians and various healthcare settings, which provides valuable insight into real-world CDI practices in Korea. However, there are several limitations. First, the survey relied on self-reported data, which may introduce recall bias. Second, the absence of patient-level data limits the ability to directly correlate clinical outcomes with reported practices. Third, the cross-sectional design captures clinical practices at a single point in time, which may not fully reflect evolving trends or responses to emerging evidence.

This study provides a detailed overview of current CDI diagnostic and treatment practices in Korea, revealing significant heterogeneity influenced by practice setting and resource availability. The rising CDI incidence in Korea, coupled with inconsistencies in diagnostic approaches and treatment adherence, underscores the need for standardized, evidence-based national guidelines tailored to Korea's healthcare environment. The recent introduction of the Korean guideline for CDI represents an important advance. However, discrepancies between guideline recommendations and real-world clinical practice persist. In particular, distinct CDI strain characteristics in Korea and limited adoption of FMT present further challenges in CDI management. Addressing these issues through comprehensive national surveillance, antimicrobial stewardship programs, and increased access to alternative treatment strategies are essential for improving CDI outcomes in Korea.

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SUPPLEMENTARY MATERIALS

Supplementary Data 1
English version of survey questionnaires

Supplementary Table 1
Survey results of opinions on the first-line treatment for non-severe and severe CDI (comparison of prescription duration)

Supplementary Table 2
Subgroup analysis by age on the selection of treatment strategies for non-severe and severe CDI

Supplementary Table 3
Survey results of opinions on the treatment for recurrent CDI regarding prescription duration

Supplementary Table 4
Subgroup analysis by age on the selection of treatment strategies for recurrent CDI.

Supplementary Fig. 1
Proposed diagnostic algorithm for *Clostridioides difficile* infection (CDI).

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