Molecular epidemiology and clinical characteristics of *Clostridioides difficile* infection in patients with inflammatory bowel disease from a teaching hospital

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Abstract

Background: *Clostridioides difficile* infection (CDI) in patients with inflammatory bowel disease (IBD) is of increasing concern. This study aimed to investigate the molecular epidemiology and antimicrobial susceptibilities of toxigenic *C. difficile* isolated from IBD patients and to evaluate the risk factors for CDI in IBD population.

Methods: Loose or watery stools from IBD patients were tested for glutamate dehydrogenase, *C. difficile* toxins A&B and anaerobic culture. Toxigenic *C. difficile* isolates were characterized by multi-locus sequence typing, ribotyping and antimicrobial susceptibility testing.

Results: The prevalence of CDI in IBD patients was 13.6% (43/317). The dominant sequence types (STs) were ST35 (20.9%), ST2 (18.6%) and ST37 (16.3%). The most common ribotypes (RTs) were RT 017 (18.6%), RT 012 (14.0%), and RT 220 (14.0%), whereas RT 027 and RT 078 were not detected in this study. All the isolates were susceptible to vancomycin and metronidazole. The multidrug resistance rate of *C. difficile* RT 017 was higher (*p* < 0.01) than that of other RT strains. Recent hospitalization, use of corticosteroids and proton pump inhibitors were related to increased risk of CDI in IBD patients; of these, recent hospitalization and proton pump inhibitors use were independent risk factors.

Conclusion: Patients with IBD have a relatively high incidence rate of CDI. *C. difficile* RT 017 is most frequently isolated from IBD patients in this region and warrants more attention to its high resistance rate. Clinicians should pay greater attention to CDI testing in IBD patients with diarrhea to ensure early diagnosis and initiation of effective treatment.

Keywords
antimicrobial resistance, *Clostridioides difficile* infection, inflammatory bowel disease, multi-locus sequence typing, ribotype, risk factors
1 | INTRODUCTION

*Clostridioides difficile* has become a major causative agent of hospital-associated and community-acquired diarrhea.\(^1\) In particular, infection with hypervirulent *C. difficile* ribotype (RT) 027 has contributed to an increase in morbidity and mortality.\(^2\) Inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), is a chronic idiopathic inflammatory gastrointestinal disorder characterized by recurring symptoms of abdominal pain, diarrhea, and bloody stools.\(^3,4\) Patients suffering from IBD are particularly susceptible to *Clostridioides difficile* infection (CDI), resulting in aggravated and deteriorating diseases, including failure of corticosteroid therapy, high risk of colectomy and high mortality.\(^5,6\) CDI may trigger IBD flares and worsen the prognosis of patients.\(^7\) Due to the overlapping clinical presentations of both conditions, clinicians must be cautious about recognizing potentially serious concurrent infection.

Current research on CDI in patients with IBD mainly focused on incidence, risk factors, treatment and prognosis, while molecular epidemiological data on toxigenic *C. difficile* from patients with IBD are relatively scarce.\(^8,9\) Thus, this study was conducted to determine the prevalence of CDI in patients with IBD, characterize the phenotype, genotype and antimicrobial resistance of toxigenic *C. difficile* isolates, and identify the risk factors associated with this infection in patients with IBD.

2 | MATERIALS AND METHODS

2.1 | Study design and patients

This was a cross-sectional study held in the Xiangya Hospital of Central South University. This is the largest tertiary hospital in Hunan Province, with more than 160,000 inpatient and 3,200,000 outpatient visits per year. A total of 317 inpatients with IBD, including 185 with CD, 123 with UC and 9 with IBD unclassified, who were admitted to the hospital from August 2016 to January 2020, were included in this study. Outpatients, repeat patients, and inpatients without diarrhea were excluded from the cohort.

2.2 | GDH and *C. difficile* toxin A&B (CDAB) testing

Loose stool samples (Bristol stool classification 5–7) from patients with IBD were simultaneously tested for GDH (ELFA, VIDAS, bioMérieux, France) and CDAB toxins (ELFA, VIDAS, bioMérieux, France) following the manufacturer's instructions.

2.3 | *C. difficile* culture and identification

Stool samples were cultured by plating on Chrome ID *C. difficile* agar medium (bioMérieux, France) after 30 min alcohol shock treatment and incubating at 37 °C for 48 hours under anaerobic conditions. Culture was considered negative if no growth was observed after 4 days incubation. Identification of *C. difficile* colonies was performed using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (Bruker Microflex LT system). The *C. difficile* isolates were stored in preservation tubes (PRO-LAB) at −80 °C.

2.4 | DNA extraction and toxin gene detection

*C. difficile* DNA was extracted using Chelex-100 as previously described.\(^10\) Afterwards, a multiplex PCR was performed to simultaneously detect 16S ribosomal DNA, tcdA (encoding toxin A), tcdB (encoding toxin B), cdtA and cdtB (encoding binary toxin), as previously described.\(^11\) If the tcdA gene was positive, further amplification that can discriminate deletion of repeating region in the tcdA gene was performed.\(^12\)

2.5 | MLST and PCR ribotyping

Seven housekeeping genes (adk, atpA, dxr, glyA, recA, sodA and tpi) of toxigenic *C. difficile* isolates were amplified according to the literature.\(^13\) The amplified products were sequenced by Sangon Biotech (Shanghai, China). The sequencing peak map was read using CHROMAS software, and the base sequences were manually compared to ensure sequencing quality. DNA sequences were queried against the PubMLST database (http://pubmlst.org/cdifficile/) to obtain allele numbers and sequence types (STs). A phylogenetic tree was constructed using the neighbor-joining (NJ) method with MEGA 7 software, and the genetic evolution of different ST strains was analyzed.

PCR ribotyping was performed by amplifying the intergenic spacer region of the 16S–23S rRNA.\(^14\) The PCR products were analyzed on genetic analyzer (ABI 3130 xl). Gene Marker V2.2.0 was used to determine the size of each peak. The results were uploaded to the WEBRIBO database (http://webribo.ages.at), and the RTs of the *C. difficile* clinical isolates were assigned.

2.6 | Antimicrobial susceptibility testing

The minimum inhibitory concentrations (MICs) of vancomycin, metronidazole, rifampicin, levofloxacin, erythromycin, clindamycin and tetracycline for *C. difficile* strains were assayed by the standard agar dilution method according to the Clinical and Laboratory Standards Institute (CLSI) guidelines (M11-A8). The above drugs were purchased from the National Institute for Food and Drug Control (Beijing, China). The drug-containing brucella agar was freshly prepared two days before use. *Bacteroides fragilis* ATCC 25285 and *C. difficile* ATCC 700057 were used as quality control strains.

MIC breakpoints for resistance to tetracycline and clindamycin were defined as ≥16 mg/L and ≥8 mg/L, respectively, according to the CLSI M100-S30 MIC breakpoint for anaerobic bacteria. MIC
breakpoints for resistance to vancomycin and metronidazole were defined as >2 mg/L, according to the EUCAST V10.0 MIC. MIC breakpoints for resistance to rifampicin, erythromycin and levofloxacin were defined as ≥4 mg/L, ≥4 mg/L, and ≥8 mg/L, respectively, according to a previous report.15

### 2.7 Clinical characteristics and risk factors analysis

The demographic and clinical characteristics of patients with IBD were obtained by reviewing their electronic medical records. The data, including age, sex, duration of hospital stay, body mass index (BMI), smoking status, alcohol drinking history, median age at IBD symptom onset, median age at IBD diagnosis, and underlying diseases (hypertension, diabetes, cardiovascular and cerebrovascular diseases, chronic liver disease, chronic kidney disease, connective tissue diseases and tumours) were collected in a blinded manner. In addition, data on hospitalization within half a year, colectomy before hospitalization, the use of antimicrobials or proton pump inhibitors (PPIs) within 1 month, and concurrent use of 5-aminosalicylate, immunomodulators, corticosteroids or anti-TNF were collected.

In addition to clinical symptoms, CDI diagnosis was based on a multistep algorithm (GDH plus toxin, arbitrated by nucleic acid amplification test).16 To evaluate the risk factors associated with CDI in the IBD population, 317 IBD patients suffering from diarrhea were classified into two groups: patients with CDI (case group) and patients without CDI (control group).

### 2.8 Statistical analysis

All data was analyzed using IBM SPSS Statistics version 25.0. Continuous variables were presented as mean ± standard deviation, non-continuous variables were presented as median and 25th and 75th percentiles and categorical variables were presented as proportions. An independent t-test or Mann–Whitney U test was used to analyze continuous variables, and the Pearson's chi-square test or Fisher's exact test was used to analyze categorical variables. Logistic regression analysis was used to identify the independent risk factors. The statistical significance value was set at p < 0.05.

### 3 RESULTS

#### 3.1 Prevalence of CDI in patients with IBD

In this study, 5.0% of patients (16/317) were positive for GDH and CDAB, yet 18.6% (59/317) were GDH positive and CDAB negative. Among 59 patients with discordant results, 45.7% (27/59) were positive for toxigenic culture. All 16 patients with positive for GDH and CDAB were found to be positive for toxigenic culture. Therefore, 43 patients with IBD were defined as CDI, including 20 patients with UC and 23 patients with CD. The prevalence of CDI in patients with IBD was 13.6% (43/317). No significant (p > 0.05) difference was found between the prevalence of CDI in patients with CD (12.4%, 23/185) and those with UC (16.3%, 20/123).

#### 3.2 Toxin typing and molecular epidemiology of the *C. difficile* isolates

Toxigenic *C. difficile* strains isolated from patients with IBD were classified into three types (Table 1): 4.7% of the strains (2/43) were A+B+CDT+, 76.7% (33/43) were A+B+CDT– and 18.6% (8/43) were A−B+CDT–.

The toxigenic *C. difficile* isolates were assigned 11 STs (Table 1). The most common type was ST35 (20.9%), followed by ST2 (18.6%), ST37 (16.3%), ST54 (14.0%), ST3 (11.6%) and ST8 (7.0%). The remaining five STs were represented by single isolate.

Fifteen RTs were identified among the 43 *C. difficile* isolates (Table 1). The predominant RT was RT 017 (18.6%), followed by RT 012 (14.0%), RT 220 (14.0%), RT 001 (11.6%), RT 006 (7.0%), RT 020 (7.0%), RT 046 (7.0%) and RT AI-75 (4.7%). The remaining seven RTs were each represented by one isolate. Hypervirulent strains (RT 027 and RT 078), usually associated with severe disease forms, were not identified in the 317 patients with IBD in this study.

A phylogenetic tree among the 43 isolates was built using the NJ method to assess the evolutionary relationships. Clade 1 was the most common branch in this study, containing 7 STs and 33 strains, followed by clade 4 and clade 3 (Figure 1). There is a correspondence between ST and RT, while one ST may contain several RTs. ST types of *C. difficile* isolated from patients with UC and CD did not show significant aggregation or predisposition.

### TABLE 1 Phenotypic and genotypic characteristics of Clostridioides difficile strains isolated from patients with IBD

| Toxin genotype (no. of isolates) | STs (no. of isolates) | Ribotype (no. of isolates) |
|----------------------------------|-----------------------|---------------------------|
| A+B+CDT+ (2)                     | ST5 (1)               | AI-56 (1)                 |
| A+B+CDT– (33)                    | ST2 (8)               | AI-58 (1)                 |
| A−B+CDT– (8)                     | ST35 (7)              | AI-75 (2)                 |
|                                  | ST37 (7)              | 017 (7)                   |
|                                  | ST375 (1)             | 017 (1)                   |

UC and 23 patients with CD. The prevalence of CDI in patients with IBD was 13.6% (43/317). No significant (p > 0.05) difference was found between the prevalence of CDI in patients with CD (12.4%, 23/185) and those with UC (16.3%, 20/123).
3.3 | Antimicrobial susceptibility analysis of *C. difficile* isolates

The MICs of the seven antimicrobial agents tested on the 43 *C. difficile* strains are presented in Table 2. All isolates were susceptible to vancomycin and metronidazole. Resistance rates to tetracycline, clindamycin, rifampicin, erythromycin and levofloxacin were 9.3%, 60.5%, 11.6%, 62.8% and 30.2%, respectively. No statistically significant differences (p > 0.05) were identified between the resistance rates of strains from CD and UC.

Different RTs and STs exhibited different antimicrobial resistance rates. The rates of resistance to tetracycline, rifampicin and levofloxacin for the RT 017 strains were significantly (p < 0.01) higher than those for the other RT strains (Figure 2A). ST37 and ST54 isolates showed significantly (p < 0.01) higher resistance rates to erythromycin than did ST2 isolates, whereas ST37 showed a higher resistance rate to levofloxacin than did ST2, ST35 and ST54 isolates (Figure 2B).

Multidrug resistance (MDR) is defined as an isolate that exhibits resistance to three or more different classes of administered antimicrobial agents. The MDR rate of the 43 strains of *C. difficile* was
The MDR rate of *C. difficile* RT 017 was 75.0% (6/8), which was higher \( p = 0.003 \) than that of other RTs strains (17.1%, 6/35).

### 3.4 Clinical characteristics and Risk factors of CDI in patients with IBD

The clinical characteristics of the IBD patients are presented in Table 3. More than 90% of patients were aged less than 60 years old, and no gender differences were observed between IBD patients with and without CDI \( p > 0.05 \). Similarly, no significant differences emerged between the two groups in terms of duration of hospital stay, BMI, colectomy before hospitalization, smoking or alcohol drinking statuses.

Univariate analysis was carried out to evaluate the risk factors associated with CDI in patients with IBD. The majority of patients did not have underlying diseases, such as hypertension, diabetes, chronic liver and kidney disease, cardiovascular or cerebrovascular diseases (Table 4). IBD patients with CDI had higher rates of recent hospitalization within half a year, concurrent use of corticosteroids and PPI use within one month \( p < 0.05 \). Multivariable logistic regression revealed that hospitalization within half a year (OR: 2.626, CI: 1.336–5.161, \( p = 0.005 \)) and use of PPIs within one month (OR: 2.393, CI: 1.070–5.351, \( p = 0.034 \)) were independent risk factors for CDI in patients with IBD (Table 4).

### 4 DISCUSSION

This study described the prevalence of CDI among IBD population in a teaching hospital in central south China. Toxigenic *C. difficile* strains isolated from patients with IBD were subjected to detailed molecular typing and drug resistance analyses, which are rarely explored in IBD population. It was found that RT 017, RT 012, RT 220 and RT 001 are the most prevalent *C. difficile* strains in patients with IBD. All isolates were susceptible to vancomycin and metronidazole. Recent hospitalization and PPI use were independent risk factors for CDI in patients with IBD.

Patients with IBD are more likely to develop CDI than the general population, which has been confirmed by previous studies.\(^{17,18}\) The prevalence of CDI in the IBD population was 13.6% in this study. As previously mentioned, the prevalence rate of CDI among intensive care patients was 8% (47/593) in same hospital as this study.\(^{19}\) The higher prevalence of CDI in patients with IBD suggests that CDI testing should be considered when IBD patients present with flare-like symptoms. The prevalence of CDI in patients with IBD in this region had not been reported before, and it ranges between 5% and 15.3% in other regions of China.\(^{20-25}\) The variation may be due to regional and study population differences; the diagnostic accuracy of the methods used in the studies may also have an impact. The methods include overly sensitive nucleic acid amplification tests and low-sensitivity enzyme immunoassays.
**TABLE 3** Demographics and clinical characteristics of IBD patients with and without CDI.

|                       | All (n = 317) | IBD with CDI (n = 43) | IBD without CDI (n = 274) | \( p \) Value |
|-----------------------|--------------|-----------------------|---------------------------|--------------|
| Age, years (mean±SD)  | 38.5±15.2    | 36.6±13.9             | 38.8±15.4                 | 0.386        |
| Gender                |              |                       |                           |              |
| Male, n (%)           | 214 (67.5%)  | 26 (60.5%)            | 188 (68.6%)               | 0.289        |
| Female, n (%)         | 103 (32.5%)  | 17 (39.5%)            | 86 (31.4%)                |              |
| IBD subtype           |              |                       |                           |              |
| CD, n (%)             | 185 (58.4%)  | 23 (53.5%)            | 162 (59.1%)               | 0.305        |
| UC, n (%)             | 123 (38.8%)  | 20 (46.5%)            | 103 (37.6%)               |              |
| IBDUK, n (%)          | 9 (2.8%)     | 0 (0.0%)              | 9 (3.3%)                  |              |
| Median age of symptom onset, years (IQR) | 31.0 (23.0–46.0) | 28.0 (23.5–44.0) | 31.0 (23.0–46.0) | 0.501 |
| Median age of IBD diagnosis, years (IQR) | 33.0 (25.0–48.0) | 31.0 (25.5–46.0) | 33.0 (25.0–49.0) | 0.581 |
| Hospitalization stay, days (IQR) | 12.0 (8.0–16.0) | 11.0 (7.0–14.0) | 12.0 (8.0–16.0) | 0.253 |
| BMI (IQR)             | 19.0 (16.7–21.4) | 19.5 (17.7–22.0) | 18.9 (16.5–21.3) | 0.218 |
| Colectomy in this hospitalization |              |                       |                           |              |
| No, n (%)             | 302 (95.3%)  | 42 (97.7%)            | 260 (94.9%)               | 0.680        |
| Yes, n (%)            | 15 (4.7%)    | 1 (2.3%)              | 14 (5.1%)                 |              |
| Smoking status        |              |                       |                           |              |
| Never, n (%)          | 250 (78.9%)  | 39 (90.7%)            | 211 (77.0%)               | 0.122        |
| Previous, n (%)       | 20 (6.3%)    | 1 (2.3%)              | 19 (6.9%)                 |              |
| Current, n (%)        | 47 (14.8%)   | 3 (7.0%)              | 44 (16.1%)                |              |
| Drinking status       |              |                       |                           |              |
| Never, n (%)          | 263 (83.0%)  | 36 (83.7%)            | 227 (82.8%)               | 0.610        |
| Previous, n (%)       | 6 (1.9%)     | 0 (0.0%)              | 6 (2.2%)                  |              |
| Current, n (%)        | 48 (15.1%)   | 7 (16.3%)             | 41 (15.0%)                |              |

Abbreviations: BMI, body mass index; IBDUK, IBD-unclassified; IQR, Inter Quartile Range.
**TABLE 4** Univariate and multivariable logistic regression analysis of risk factors for *Clostridioides difficile* infection in patients with IBD

| Risk Factor                              | Total (n = 317) | IBD with CDI (n = 43) | IBD without CDI (n = 274) | Univariate analysis | Multivariate analysis |
|------------------------------------------|-----------------|-----------------------|---------------------------|---------------------|----------------------|
| Hospitalization within half a year, n (%) | 130 (41.0%)     | 27 (62.8%)            | 103 (37.6%)               | 9.756               | 2.626 (1.336–5.161)   |
| colectomy before this hospitalization, n (%) | 23 (7.3%)      | 3 (7.0%)              | 20 (7.3%)                 | 0                   | 1                    |
| Hypertension, n (%)                      | 10 (3.2%)       | 3 (7.0%)              | 7 (2.6%)                  | 1.152               | 0.283                |
| Diabetes mellitus, n (%)                 | 2 (0.6%)        | 0 (0.0%)              | 2 (0.7%)                  | 0                   | 1                    |
| Chronic liver diseases, n (%)            | 10 (3.2%)       | 2 (4.7%)              | 8 (2.9%)                  | 0.018               | 0.893                |
| Chronic kidney diseases, n (%)           | 0 (0.0%)        | 0 (0.0%)              | 0 (0.0%)                  | /                   | /                    |
| Cardio-cerebrovascular diseases, n (%)   | 11 (3.5%)       | 1 (2.3%)              | 10 (3.6%)                 | 0                   | 1                    |
| Connective tissue diseases, n (%)        | 0 (0.0%)        | 0 (0.0%)              | 0 (0.0%)                  | /                   | /                    |
| Tumor, n (%)                             | 1 (0.3%)        | 0 (0.0%)              | 1 (0.4%)                  | 0                   | 1                    |
| Concurrent use of 5-aminosalicylate, n (%) | 173 (54.6%)    | 22 (51.2%)            | 151 (55.1%)               | 0.234               | 0.629                |
| Concurrent use of corticosteroids, n (%) | 46 (14.5%)      | 11 (25.6%)            | 35 (12.8%)                | 4.915               | 1.988 (0.892–4.432)   |
| Concurrent use of Immunomodulators, n (%) | 28 (8.8%)      | 5 (11.6%)             | 23 (8.4%)                 | 0.165               | 0.685                |
| Concurrent use of anti-TNF, n (%)        | 28 (8.8%)       | 5 (11.6%)             | 23 (8.4%)                 | 0.165               | 0.685                |
| antibiotics use within 1 month, n (%)    | 68 (21.5%)      | 9 (20.9%)             | 59 (21.5%)                | 0.008               | 0.929                |
| PPIs use within 1 month, n (%)           | 43 (13.6%)      | 11 (25.6%)            | 32 (11.7%)                | 6.127               | 2.393 (1.070–5.351)   |

Abbreviation: CI, confidence interval.

*, P < 0.05; **, P < 0.01.

*Clostridioides difficile* genotypes are distributed geographically across nations and regions. RT 027 and RT 078 are most frequently isolated in Europe and North America.26,27 RT 017 is more prevalent in Asia, and there have been few reports of the RT 017 strain in other regions of the world so far.28 The most prevalent RTs of *C. difficile* strains isolated from patients with IBD in this study are similar to that found in the general population in our previous study.29 It was found that the dominant RTs were RT017, RT046, and RT012 in patients hospitalized with diarrhea between 2009 and 2010 in the same hospital.

Based on the antimicrobial susceptibility test, all clinical isolates from patients with IBD proved susceptible to vancomycin and metronidazole. There was a relatively low resistance rate to tetracycline and rifampicin compared with the high resistance rate to erythromycin, clindamycin and levofloxacin. Some studies have shown that high resistance to ciprofloxacin and clindamycin is commonly observed in *C. difficile* isolates.30–32 As one of the most common RT from patients with IBD, *C. difficile* RT 017 exhibited a higher MDR rate than other RT strains in this study. *C. difficile* RT 017 is always associated with antimicrobial resistance and may increase the risk of future spread or outbreaks, and may make CDI treatment more challenging.33 Therefore, it is necessary to carry out molecular typing of *C. difficile* strains, which is meaningful for epidemiological surveillance and clinical treatment.

In this study, most patients with IBD were younger than 60 years old and the comorbidity burden rate was very low, which is different from the general CDI population.34–36 In the general population, clindamycin, extended-spectrum cephalosporins and fluoroquinolones have been reported to be associated with CDI.35 Similar antibiotics were prescribed in 21.5% of IBD cases in this study. However, there was no significant difference in antimicrobial agent use between the case group and control group, which may be partly explained by the different population.

Recent hospitalization, use of corticosteroids and proton pump inhibitors were related to the increased risk of CDI in patients with IBD in this study. Similarly, recent hospitalization has been identified as a risk factor for CDI in other studies.23,37 Hospitalization may increase exposure to *C. difficile* spores, as well as the likelihood of medication. Corticosteroids are effective for the induction of rapid remission of IBD symptoms; however, long-term use of these drugs does not provide complete relief and may produce many adverse effects, including a risk of increased mortality.38 Published data demonstrate that exposure to corticosteroids is associated with an increased risk of CDI37 and with a higher risk of colon surgery3 in patients with IBD. In this study, the IBD patients with CDI used corticosteroids more frequently than those without CDI, and yet corticosteroids use was not an independent risk factor for CDI. This finding reveals that clinicians should be more cautious about initiating or
escalating systemic steroids when patients experience clinical deterioration and CDI has not been ruled out.

Increasing evidence exists for a strong association between PPI use and CDI. Research by Malin et al. has already found that there is a significant association between PPI exposure and increased risk of community-associated CDI, and the risk persists for 6–12 months even if PPI treatment has ended. Previous studies have explored the association between PPI use and risk of CDI in patients with IBD, but the conclusions have not been consistent.²³,²⁴ This study identified that the use of PPI is an independent risk factor for CDI in patients with IBD. It remains unclear how PPIs contribute to the increase in the risk of CDI and there may be multiple mechanisms underlying the association. PPIs reduce the protective effect of gastric acid by up-regulating gastric pH. This may predispose bacterial overgrowth and dysbiosis, which increases the survival of spores and vegetative form of C. difficile.⁴¹,⁴² Additionally, PPIs have been shown to enhance C. difficile toxin expression and inhibit neutrophil activity.⁴³

There are some limitations to be considered in this study. This is a single-center study, and the findings might not be adequately representative of the entire region or other countries. Moreover, some information was limited and incomplete in the retrospective collection of clinical data from the electronic medical record system. In the future, additional multicenter or prospective studies should be conducted to explore the pathogenesis and interplay of CDI in patients with IBD.

5 | CONCLUSIONS

In conclusion, the incidence of CDI is relatively high in patients with IBD. Clostridioides difficile RT 017 is most frequently isolated from patients with IBD in this region and warrants more attention to its high resistance rate. Screening tests for CDI should be performed in IBD patients with diarrhea, especially in those with a recent history of hospitalization and exposure to PPIs and corticosteroids.

AUTHOR CONTRIBUTIONS

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Yan-ming Li, Jing-zhong Liao, Zi-juan Jian, Hong-ling Li, Xiao Chen, Qing-xia Liu, Pei-lin Liu, Zhi-juan Wang, Xuan Liu, Qun Yan and Wen-en Liu. The first draft of the manuscript was written by Yan-ming Li and the final review was done by Wen-en Liu and Qun Yan. All authors read and approved the final manuscript.

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CONFLICT OF INTEREST

The authors report no conflicts of interest in this work.

DATA AVAILABILITY STATEMENT

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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