Characteristics of Clostridioides difficile infection in inflammatory bowel disease

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Research

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Abstract

Background: The epidemiology of *Clostridioides difficile* infection(CDI) in China is different from western countries and the characteristics of CDI among inflammatory bowel disease (IBD) in China may be unique. The aim of this study was to investigate the molecular epidemiology and to find out the risk factors of CDI among IBD inpatients in Jiangsu Province, China.

Methods: Patients with IBD admitted to the First Affiliated Hospital with Nanjing Medical University from August 2013 to December 2018 were enrolled. IBD patients were matched with non IBD patients according to age and gender. Diarrhea samples were sent for CDI diagnosis and the molecular epidemiology investigation was performed. Finally, patients' information was collected and logistic regression analysis was performed to analyze the independent risk factors of CDI in IBD patients.

Results: In this study, the incidence of CDI in IBD patients was much higher than that in non IBD patients (24.6% vs. 9.0%) and community acquired infection was the main kind. The predominant type of epidemic strain of *C. difficile* in this study was ST54. The shorter history of IBD and recent use of quinolone antibiotics were independent risk factors for CDI among diarrhea patients with IBD.

Conclusion: If the duration of IBD is within one year or quinolone antibiotics have been used recently, clinicians should consider the possibility of IBD patients complicated with CDI and adjust the treatment plan.

Background

Clostridioides difficile (*C. difficile*) is a kind of gram-positive spore-forming anaerobe bacillus. In 1978, *C. difficile* was found to be associated with pseudomememous enteritis and antibiotic-associated diarrhea[1]. The symptoms of *Clostridioides difficile* infection (CDI) include asymptomatic carriers, diarrhea, toxic megacolon and even death. In America, the status of *C. difficile* has exceeded methicillin-resistant *Staphylococcus aureus* (MRSA) and has become the major cause of nosocomial infection[2, 3]. In mainland China, the incidence of CDI in diarrhea patients is about 14%[4]. Moreover, the hypervirulent strain (NAP1/RT027) has been scatterly reported in China[5, 6]. On the other hand, the incidence of inflammatory bowel disease (IBD) in China has been increasing recently and it has become a common cause of digestive system disease including chronic diarrhea. More and more studies have shown that intestinal microecological imbalance, such as the decrease of beneficial bacteria and their metabolites in the intestinal tract and the increase of harmful bacteria and their metabolites, may change the intestinal environment, thus causing IBD. And this process is very similar to the occurrence and development of CDI[7]. However, it is not clear whether there is a causal relationship between CDI and IBD. Most studies have reported that IBD is an independent risk factor for CDI even in the absence of other factors, such as antibiotics and long-term hospitalization[8–10]. Additionally, more and more studies found an increasing incidence of CDI among patients with IBD and this kind of parients commonly had a more severe course of disease than non IBD population[9, 11–13].

In western countries, CDI is considered to be the main cause of hospital-acquired infections and the detection of CDI is widely performed. However, in China, due to the high nutritional requirements, anaerobic culture and the high cost of toxin detection, only some teaching hospitals carry out the project of CDI and physicians usually ignore this issue. Compared with western countries, such as Europe and the United States, China has its own social characteristics, such as aging population and extensive use of antibiotics, which are the rik factors of CDI. So, the molecular epidemiology of CDI among diarrhea patients with IBD in China may be unique. However, the incidence and risk factors of CDI among Chinese IBD patients are still poorly characterized. Therefore, we performed this study to investigate the molecular epidemiology and risk factors of CDI among hospitalized diarrhea patients with IBD in Jiangsu Province, China.

Methods

Patients

Adult patients with IBD hospitalized in the First Affiliated Hospital with Nanjing Medical University between August 2013 and December 2018 were enrolled in the current study. The inclusion criteria for IBD patients were as follows: (1) hospitalized IBD patients with ulcerative colitis (UC) or Crohn's disease (CD) within the study period; (2) at least 16 years of old; (3) with an increase of at least three loose and watery stools per day. To compare the incidence of CDI between IBD inpatients and non IBD inpatients, non IBD inpatients were mateched with IBD inpatients one by one according to gender and age (within 1 year). Patients with normal feces and incomplete information were excluded. This study was approved by the hospital ethics committee.

Detection of CDI

A case of CDI was defined on the basis of the presence of symptoms (usually diarrhea) and successful isolation of *C. difficile* with a positive PCR test for toxin genes. Toxigenic culture was performed as the standard diagnostic test for CDI[14, 15]. Isolation and toxin genes detection of *C. difficile* were perfprmed as we reported before[16]. Briefly, *C. difficile* was isolated from all loose or watery fecal samples with cefoxitin-cycloserine fructose agar plates (BioMérieux, France) under anaerobic conditions. Suspected clones were further identified by VITEK 2 ANC cards (BioMérieux, France). Bacterial genomic DNA was extracted from the identified colonies using the TIANamp Bacteria DNA Kit (TIANGEN Biotech, Beijing, China) according to the manufacturer's instructions. Then, *tcdA*, *tcdB*, and binary toxin (*cdtA/cdtB*) genes were amplified and analyzed as previously described[17]. ATCC BAA-1870 was positive control and ATCC 700057 was negative control. All isolated strains and extracted necleic acid were frozen at − 70 °C for further study.

Multilocus sequence typing (MLST)

To investigate the molecular epidemiology, MLST was performed as described previously by Griffiths et al[18]. The *adk*, *atp*A, *dxr*, *gly*A, *rec*A, *sod*A, and *tpi* housekeeping genes were targeted. ATCC BAA-1870

was positive control. The amplified products were sent to Sangon Biotech (Shanghai, China) for sequencing. Then, the DNA sequences of the 7 genes were submitted to the MLST database (http://pubmlst.org/cdifficile) to get the sequence type (ST). The specific primers for toxin genes and housekeeping genes are shown in Table 1. The corresponding PCR characterizations are shown in Fig. 1 and Fig. 2, respectively.

Table 1
Primers used for toxin genes and housekeeping genes of *C. difficile*

Gene	Primer	Nucleotide sequence(5'–3')	Fragment length(bp)
tcdA	tcdA-F3345	GCATGATAAGGCAACTTCAGTGGTA	625
	tcdA-R3969	AGTTCCTCCTGCTCCATCAAATG	
tcdB	tcdB-F5670	CCAAARTGGAGTGTTACAAACAGGTG	410
	tcdB-R6079B	GCATTTCTCCGTTTTCAGCAAAGTA	
cdtA	cdtA-F739A	GGGAAGCACTATATTAAAGCAGAAGC	221
	cdtA-R958	CTGGGTTAGGATTATTTACTGGACCA	
cdtB	ctdB-F617	TTGACCCAAAGTTGATGTCTGATTG	262
	ctdB-R878	CGGATCTCTTGCTTCAGTCTTTATAG	
adk	adk1F	TTACTTGGACCTCCAGGTGC	501
	adk1R	TTTCCACTTCCTAAGGCTGC	
*atp*A	atpA1F	TGATGATTTAAGTAAACAAGCTG	555
	atpA1R	AATCATGAGTGAAGTCTTCTCC	
dxr	dxr3F	GCTACTTTCCATTCTATCTG	411
	dxr4R	CCAACTCTTTGTGCTATAAA	
*gly*A	glyA1F	ATAGCTGATGAGGTTGGAGC	516
	glyA1R	TTCTAGCCTTAGATTCTTCATC	
*rec*A	recA2F	CAGTAATGAAATTGGGAGAAGC	564
	recA2R	ATTCAGCTTGCTTAAATGGTG	
*sod*A	sodA5F	CCAGTTGTCAATGTATTCATTTC	450
	sodA6R	ATAACTTCATTTGCTTTTACACC	
tpi	tpi2F	ATGAGAAAACCTATAATTGCAG	504
	tpi2R	TTGAAGGTTTAACACTTCCACC	

Data collection

Clinical data were obtained through the inpatient medical record system, including the length of stay (LOS), submission date, gender, age, diagnosis, stool consistency, history of IBD and so on. Potential risk factors(3 months before the detection of CDI), including treatment with antibiotics, systemic steroids, oral 5-aminosalicylic acid (5-ASA) and proton pump inhibitor (PPI) were classified as positive or negative, respectively. If IBD patients were complicated with CDI, metronidazole and ornidazole were mostly used to treat CDI. Laboratory test indexes during the hospitalization were also collected.

Statistical analysis

All data were analyzed using SPSS 22.0 statistical software (SPSS, Chicago, IL, USA). Continuous variables were analyzed by Student's *t* test or Wilcoxon Rank Sum test, depending on whether data were normally distributed. In this study, age was analyzed by Student's *t* test and the length of stay was analyzed by Wilcoxon Rank Sum test. Categorical variables were expressed by frequencies and compared through χ^2 test. Univariate and multivariate logistic regression were used to identify the independent risk factors for CDI among patients with IBD. Odds ratios (OR) and 95% confidence interval (95%CI) were calculated for risk factors to quantify the strength of these associations. Also, $P < 0.05$ was considered statistically significant.

ResutIts

Demographics and Characteristics

A total of 193 cases of IBD patients were confirmed. Patients who did not meet the inclusion criteria were excluded and 134 cases were enrolled in this study finally, including 84 patients with UC and 50 patients with CD. Of these patients, 85 were male and 49 were female. The mean age of IBD patients was 42 years of old and CD patients were much younger than UC patients. The median LOS in CD group was 6 days while the median LOS in UC group was 9 days. There was no statistical significance in terms of gender, antibiotics and PPI between CD patients and UC patients. Also, we found 134 cases of non IBD diarrhea patients as matched group. Although the LOS in IBD group was shorter than that in non IBD group, the incidence of CDI in IBD group was much higher than that in non IBD group and the difference was statistically significant. More details were described in Table 2.

Table 2
Demographics and characteristics of patients with or without IBD

Factors	IBD n = 134	No IBD n = 134	*P*	CD n = 50	UC n = 84	*P*
Age,yrs[Mean (range)]	42.1(16–83)	42.4 (16–83)	0.867[a]	31.7 (16–56)	48.2 (19–83)	< 0.001[a]*
Male [N (%)]	85 (63.4%)	85 (63.4%)	1	37 (74.0%)	48 (57.1%)	0.05
LOS[median (quartile)]	8 (5-13.5)	10 (5-23.25)	0.013[b]*	6 (5-10.25)	9 (6–16)	0.009[b]*
CDI	33(24.6%)	12(9.0%)	0.001*	16(32%)	17(20.2%)	0.126
Antibiotics	47(35.1%)	62(46.3%)	0.062	17(34%)	30(35.7%)	0.841
Cephalosporin	36(26.9%)	32(23.9%)	0.574	12(24%)	24(28.6%)	0.564
Quinolones	17(12.7%)	10(7.5%)	0.155	5(10%)	12(14.3%)	0.471
PPI	28(20.9%)	21(15.7%)	0.105	6(12%)	22(26.2%)	0.051

[a] Student's *t* test, [b] Wilcoxon Rank Sum test, others are χ^2 test, * $P < 0.05$

Incidence of CDI in IBD patients

In total, 33 (24.6%) non-duplicate toxigenic *C. difficile* isolates were identified from 134 IBD patients suffering from diarrhoea while 12 (9.0%) cases of CDI were confirmed among matched non IBD patients. Toxigenic *C. difficile* isolates were both *tcdA* and *tcdB* positive and no binary toxin positive strain was isolated in this investigation. There were 4 toxin genes negative strains isolated from UC and CD groups, respectively. More details were described in Fig. 3 and Fig. 4. The incidence of CDI in CD group was 32.0% (16/50) while the incidence of CDI in UC group was 20.2% (17/84). However, there was no statistically significant about the incidence between CD and UC group. On the other hand, the incidence of CDI in IBD group was significantly higher than the matched non IBD group. In Fig. 5, the detection rates of CDI in CD and UC group were both higher than the mached groups, respectively.

MLST and source of CDI

After MLST analysis, 33 toxigenic *C. difficile* isolations from IBD patients could be classified into 9 sequence types (ST). The most prevalent type was ST54 (27.3%, 9/33), followed by ST3 (21.2%, 7/33). The hypervirulent *C. difficile* strain ST1 (NAP1/B1/027) was not found in our study. ST54 and ST3 accounted for almost half of the toxigenic *C. difficile* isolations from diarrhea inpatients with IBD in our hospital. In addition, two-thirds of CDI in IBD patients are community-acquired infection (22/33) and nosocomial infections only accounted for 33.3% (11/33). More details were listed in Table 3 and Fig. 6.

Table 3
Source of CDI and stool consistency at discharge

Code	Admission time	Isolation time	Hospital-acquiredCDI	MLST	Type	Antibiotics	Stool consistency at discharge
CDF1	20131006	20131023	Yes	ST35	UC	No	diarrhea
CDF2	20131023	20131024	No	ST37	UC	LVX + ONZ	loose stool
CDF3	20140120	20140122	No	ST54	UC	No	normal
CDF4	20140218	20140225	Yes	ST26	CD	TNZ	normal
CDF5	20140625	20140626	No	ST37	UC	ONZ	normal
CDF6	20140624	20140702	Yes	ST54	UC	No	loose stool
CDF7	20151123	20151124	No	ST35	CD	No	normal
CDF8	20160712	20160714	No	ST54	UC	No	mucous stool
CDF9	20160714	20160715	No	ST3	CD	No	loose stool
CDF10	20160917	20160921	Yes	ST37	CD	No	normal
CDF11	20160928	20161002	Yes	ST54	CD	No	diarrhea
CDF12	20161010	20161010	No	ST54	UC	No	diarrhea
CDF13	20161116	20161118	No	ST54	CD	MET	normal
CDF14	20170209	20170210	No	ST54	CD	MET	normal
CDF15	20170403	20170404	No	ST35	UC	MET	normal
CDF16	20170403	20170404	No	ST14	UC	No	normal
CDF17	20170503	20170504	No	ST2	UC	No	normal
CDF18	20170505	20170505	No	ST42	UC	ONZ	normal
CDF19	20170519	20170523	Yes	ST2	CD	No	diarrhea
CDF20	20170520	20170524	Yes	ST15	UC	No	normal
CDF21	20170523	20170524	No	ST35	UC	MET	normal
CDF22	20170527	20170530	Yes	ST37	CD	MET	normal
CDF23	20170721	20170722	No	ST3	UC	No	normal
CDF24	20170727	20170728	No	ST35	CD	No	normal
CDF25	20170905	20170906	No	ST2	CD	No	normal

MET metronidazole, TNZ tinidazole, ONZ ornidazole, LVX levofloxacin

Code	Admission time	Isolation time	Hospital-acquiredCDI	MLST	Type	Antibiotics	Stool consistency at discharge
CDF26	20171005	20171011	Yes	ST54	CD	No	loose stool
CDF27	20180105	20180106	No	ST2	CD	MET	normal
CDF28	20180319	20180320	No	ST54	CD	No	diarrhea
CDF29	20180412	20180413	No	ST3	CD	No	normal
CDF30	20180726	20180813	Yes	ST3	UC	ONZ	normal
CDF31	20180808	20180816	Yes	ST3	UC	No	normal
CDF32	20181126	20181127	No	ST3	CD	MET	normal
CDF33	20181228	20181228	No	ST3	UC	LVX + ONZ	normal
MET metronidazole, TNZ tinidazole, ONZ ornidazole, LVX levofloxacin							

Risk factors of CDI in IBD patients

The effects of CDI associated risk factors, including age, gender, history of IBD, antibiotics, PPI, LOS and so on. The antibiotics uesd in this study were mainly the third generation cephalosporin and levofloxacin. In Table 4, we could found that quinolones and the first year after diagnosis of IBD have statistics significance ($P < 0.01$). Than, after multivariate logistic regression analysis, these variables were confirmed to be the independent risk factors for CDI among diarrha inpatients with IBD. In Table 5, we discoved that patients with IBD who had a history within one year were about 2.7 times more likely to develop CDI than those with a history of more than one year. What's more, IBD patients who recently used quinolones were about 3 times more likely to develop CDI than those who did not. However, PPI, 5-ASA and systemic steroids were not related to CDI rate. Also, CDI seems to be not associated with older age and longer hospitalization among diarrhea patients with IBD.

Table 4
Characteristics of IBD patients with or without CDI

Factors	CDI n = 33	NC n = 101	*P*
Male [N (%)]	19(57.6%)	66(65.3%)	0.421
Age,yrs[Mean (range)]	41.1(17–82)	42.4 (16–83)	0.694[a]
LOS[median (quartile)]	6(4–13)	8 (5-13.5)	0.143[b]
History of IBD within 1 year	22(66.7%)	38(37.6%)	0.004*
Treatments			
Antibiotics	13(39.4%)	34(33.7%)	0.549
Cephalosporin	10(30.3%)	26(25.7%)	0.608
Quinolones	9(27.3%)	8(7.9%)	0.007[c]*
5-ASA	28(84.8%)	79(78.2%)	0.410
PPI	8(24.2%)	20(19.8%)	0.586
systemic steroids	6(18.2%)	26(25.7%)	0.376
Laboratory test indexes			
CRP(>8 mg/ml)	23(69.7%)	70(69.3%)	0.966
Hypocalcemia	13(39.4%)	44(43.6%)	0.674
Anemia	21(63.6%)	63(62.4%)	0.897

NC without CDI, [a] Student's *t* test, [b] Wilcoxon Rank Sum test, [c] *Fisher* test, others are χ^2 test, * $P < 0.05$

Table 5
Multivariate Analysis of Risk Factors for CDI among IBD patients

Factors	*P*	OR	95%CI
History of IBD within 1 year	0.026	2.669	1.123–6.344
Quinolones	0.048	3.048	1.011–9.190

Stool consistency at discharge

In addition to routine treatment for IBD, not all IBD patients complicated with CDI received antiobitic treatment for CDI in this study. Metronidazole and ornidazole were mostly used to treat CDI. In Table 3, 13 patients received antibiotics targeted *C. difficile* and only 1patient still had loose stool at discharge. However, 20 patients only treated IBD alone and no antiobitic was taken to treat CDI. When discharged,

only 11 patients recovered from diarrhea and the rest of them still had some issues, for example, 1 patient had mucous stool, 3 patients had loose stool, and 5 patients still had diarrhea.

Discussion

CDI has become a major public health problem. In United States, CDI causes about 450,000 infections and 35,000 deaths each year and *C. difficile* is also the major cause of hospital acquired infections in UK[19, 20]. Aging population and widely use of antibiotics are the current social situation in China, which can increase the risk of CDI. According to one meta-analysis by our early work, the incidence of CDI among hospitalized diarrhea patients is about 14% in mainland China[4]. Among IBD patients, the infection rate of *C. difficile* has been increasing steadily over the past decades[8, 21]. IBD is proven to be an independent risk factor for CDI. Moreover, IBD populations complicated with CDI usually have worse outcome[22]. In this study, the incidence of CDI among IBD patients was 24.6% (33/134) and was much higher than matched non IBD group. According to our knowldege, the infection rate of *C. difficile* in patients with IBD most studies reported in western countries is less than 10% and was much lower than this investigation[23, 24]. The method they used to detect CDI was toxigenic culture or an algorithm, including glutamate dehydrogenase (GDH) and *C. difficile* toxin A or B (CDAB) with nucleic acid amplification testing (NAAT) as confirmatory test, respectively. The method we used in this study was also toxigenic culture. The rates of CDI between our study and thier researches are comparable. However, while camparing the incidence of our study with other data in China, only few studies about the epidemiology of CDI among IBD patiens in China were searched. One study from Peking Union Medical College Hospital reported that thay identified 60 (7.41%) cases of CDI among 810 patients with IBD[25]. However, the method they used to detect CDI is enzyme immunoassay (EIA)-based stool test results for CDAB. It is widely reported that the low sensitivity of this method detecting free toxin in stool ranges from 32%–79%[26–28]. This may leads to the incidence of CDI on the low side. In our study, we also used VIDAS® *C. difficile* panel (BioMérieux, France) to detect partial diarrhea samples. Among 29 cases of toxigenic *C. difficile* diarrhea samples detected by toxigenic culture, only 6 cases were positive and 2 cases were suspected for CDAB from diarrhea samples detected by EIA method. The rest test reselts were all negative. The sensitivity of CDAB for CDI detection compared with toxigenic culture is only 27.6% (8/29), even including the suspicious positive cases. Although the number of CDI cases included in this study for CDAB test was small, it could also reflect the issue to some extent. So, the real incidence of CDI in hspitalized diahhrea patients with IBD may be higher in China and our data could fill the gap in this field to a certain extent. In this study, about two thirds of CDI among IBD patients were community acquired infections and nosocomial infections only accounted for 33.3% (11/33). According to the research of Rodemann JF and his colleagues, nearly two-thirds of IBD patients with CDI were community acquired infection, which was consistent with our result[21]. Community acquired infection accounts for the majority of CDI among diarrhea inpatients with IBD.

In addition, no binary toxin positive strains were isolated in this study and all toxigenic strains were both positive for *tcdA* and *tcdB* and there was no report about the hypervirulent strain RT027 isolated from IBD patients in China as far as we know. ST54 was the main type of toxigenic *C. difficile* among diarrhea

patients with IBD. After MLST analysis, we discovered that ST54 and ST3 accounted for nearly half of the toxigenic isolations from patients with IBD in this study. Meanwhile, many literatures reported that ST54 was widely distributed in the world and was detected in Japan, India, Chile and other places[29]. It has also been reported that ST54 occupies the second place of CDI in domestic pregnant women[30]. Recently, investigations carried out in Chinese hospitals revealed that ST54 was the predominant type of CDI in diarrhea patients[31, 32]. Also, according to our previous meta-analysis about the domestic molecular epidemiology, the epidemic strain of *C. difficile* isolated from diarrhea patients were mainly ST3, ST37 and ST54, accounting for 18.1%, 17.2% and 16.7%, respectively. This indicates that ST54 strain plays an important role not only in IBD patients, but also in other populations.

It is widely acknowledeged that broad-spectrum antibiotics, proton pump inhibitors, older age, immunosuppressants and long-term hospitalization are all related to the occurrence and development of CDI[33–35]. However, the incidence of CDI among patients with IBD is still very high even if they have not used antibiotics recently and have not been exposed to the medical environment[36]. Compared with the general population, IBD seems to be an independent risk factor for CDI. This may be caused by the imbalance of gastrointestinal and immune functions, intestinal flora disorders, intestinal epithelial damage and other factors in IBD patients. The differences and associations about the risk factors for CDI between IBD patients and the general population deserve further study. In this study, the independent risk factors for CDI among IBD patients were the recent use of quinolones and the first year after initial diagnosis of IBD. In this study, levofloxacin was the mainly uesd quinolones. Quinolones have been widely recognized as an independent risk factor for CDI and our study confirmed that quinolones remaind a risk factor for CDI among diarrhea patients with IBD. Singh H and his colleagues reported the highest rates of CDI within the first year of IBD diagnosis and shorter duration of IBD was associated with an increased risk of CDI[13]. This may be explained by the higher rates of dysbiosis of gut flora at IBD diagnosis, untreated altered humoral immune responses, or epithelial dysfunction predisposing to CDI. Interestingly, many studies about the independent risk factors for CDI in IBD patients discovered that steroids, biologics and immunomodulators, which have been widely considered as risk factors for CDI, have not been associated with the higher incidence of CDI in IBD patients[24, 37, 38]. In our study, systemic steroids were not associated with CDI susceptibility in patients with IBD. There is no consensus on the independent risk factors for CDI among IBD patients at present. Different studies often come to different conclusions, such as recent use of antibiotics, admission to hospital, PPI and so on[23, 24, 37, 39].

Also, this study did not find that IBD patients complicated with CDI extended the length of hospital stay, which was consistent with the results of multiple single-center studies[8, 40]. One investigation carried out in USA discovered that more than half of the infected IBD patients required hospitalization and 20% required colectomy. However, only several cases in this study accepted colectomy. Two studies from Europe reported the rate of colectomy was about 5%. There is still controversy over whether CDI increases the rate of colectomy among patients with IBD. High quality researches are needed to resolve this issue.

What's more, almost all infected IBD patients who received CDI treatment were recovered from diarrhea in this study (12/13) while almost half of the untreated CDI patient still had issues with stool (9/20), even 5 cases still had diarrhea when they were at discharge. This indicates the conventional therapy of IBD does not apply to patients complicated with CDI and emphasizes the importance of early diagnosis and targeted treatment against CDI.

Despite the discoveries in this study, there are some limitations should be considered. Firstly, this single-center study was conducted in a tertiary care university teaching hospital and the sample size enrolled in this study was insufficiently large. For example, when analysis the clinical characteristics of IBD patients with or without CDI, cases of some variables are limited. In-depth subgroup analysis about the incidence of CDI among different characteristics of IBD could not be performed. Secondly, not all diarrhea amples used CDAB to detect CDI because this panel was used in our hospital not from the beginning of this study and we could not compare the incidence of CDI with the data from the Beijing, China[25]. Addiotionally, not all diarrhea inpatients sent stool for CDI detection within 48 h after admission and the true proportion of community-acquired CDI maybe higher than the data we received. Last but not least, we did not follow up the enrolled patients because part patients were from other cities and lost to follow up.

Conclusions

Although no hypervirulent strain RT027 was detected in this study, the incidence of CDI in IBD patients in our hospital was significantly higher than that in most western countries. Community acquired infection was the main type of CDI and ST54 was the epidemic strains among IBD patients in China. In addition, if the duration of IBD is within one year or quinolone antibiotics have been used recently, clinicians should consider the possibility of IBD patients complicated by CDI and adjust the treatment plan.

Abbreviations

CDI
Clostridioides difficile infection
IBD
inflammatory bowel disease
MRSA
methicillin-resistant *Staphylococcus aureus*
UC
ulcerative colitis
CD
Crohn's disease
MLST
multilocus sequence typing
ST
sequence type

LOS
length of stay
5-ASA
5-aminosalicylic acid
PPI
proton pump inhibitor
OR
odds ratios
GDH
glutamate dehydrogenase
CDAB
C.difficile toxin A or B
NAAT
nucleic acid amplification testing

Declarations

Availability of data and materials

All data generated and analyzed during this study were included in this published article.

Ethics approval and consent to participate

This study was approved by the hospital ethics committee.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Author Contributions

Genyan Liu and Chenjie Tang devised the study. Chengcheng Liu, Yaping Han and Chenjie Tang collected the specimens and/or performed the experiments. Xiaohui Zhang and Wenying Xia collected and analysed data. Chenjie Tang, Fang Ni and Genyan Liu drafted the manuscript. All authors contributed to and approved the final version.

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Figures

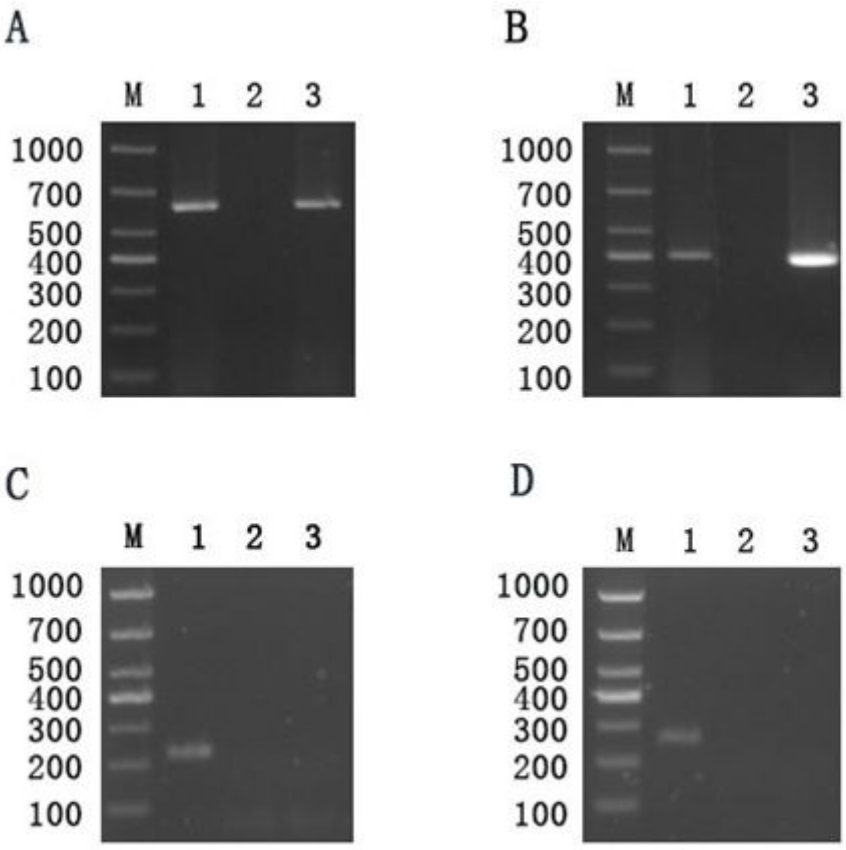

Figure 1

PCR products of C. difficile toxin genes. (A) PCR products of tcdA (625bp), (B) PCR products of tcdB (410bp), (C) PCR products of cdtA (221bp), (D) PCR products of cdtB (262bp), M molecular marker, 1 positive control, 2 negative control, 3 clinical samples

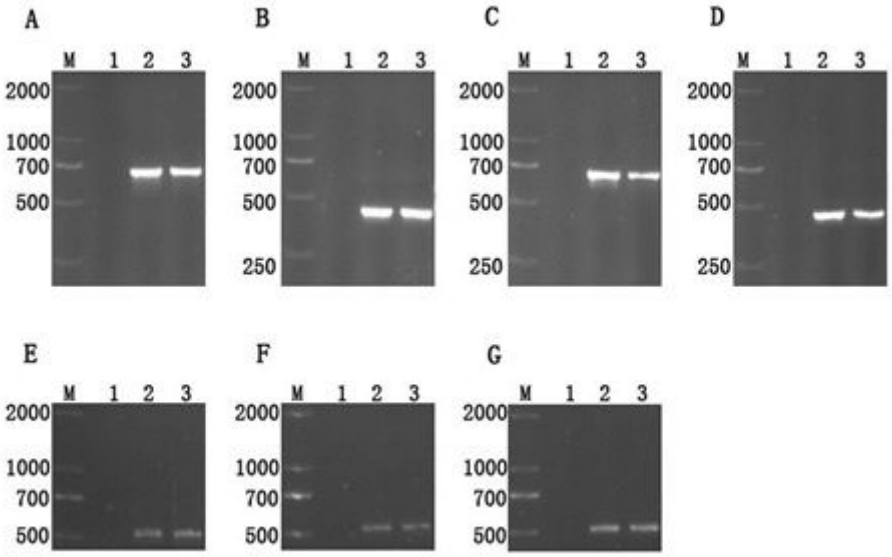

Figure 2

PCR products of C. difficile MLST. (A) PCR products of atpA (555bp), (B) PCR products of dxr (411bp), (C) PCR products of recA (564bp), (D) PCR products of sodA(450bp), (E) PCR products of adk (501bp), (F) PCR products of glyA(516bp), (G) PCR products of tpi (504bp), M molecular marker, 1 negative control, 2 positive control, 3 clinical samples

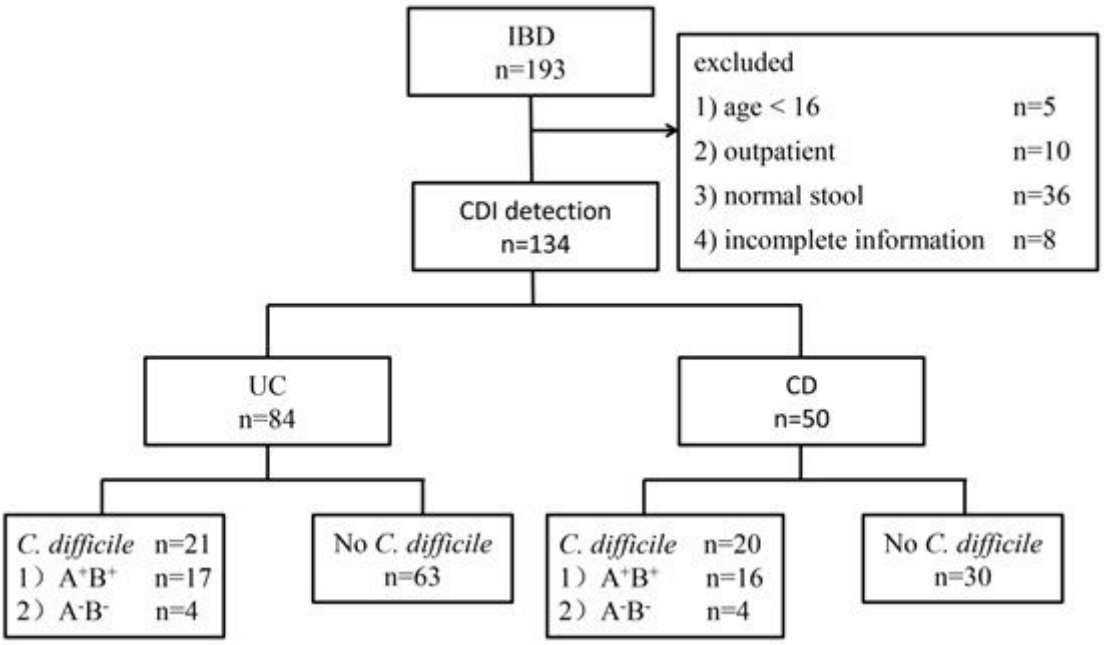

Figure 3

Overview diagram of the detcetion of CDI in IBD patients. A+B+ positive results of tcdA and tcdB, A-B- negative reslults of tcdA and tcdB

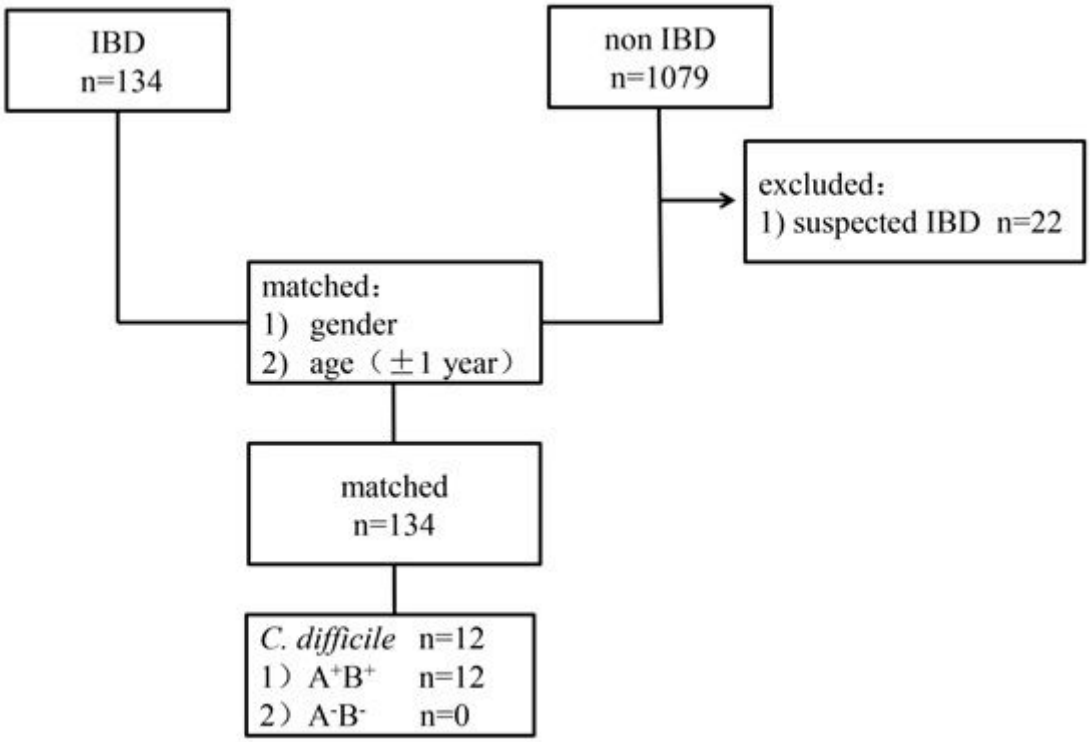

Figure 4

Overview diagram of the detcetion of CDI in non IBD patients. A+B+ positive results of tcdA and tcdB, A-B- negative reslults of tcdA and tcdB

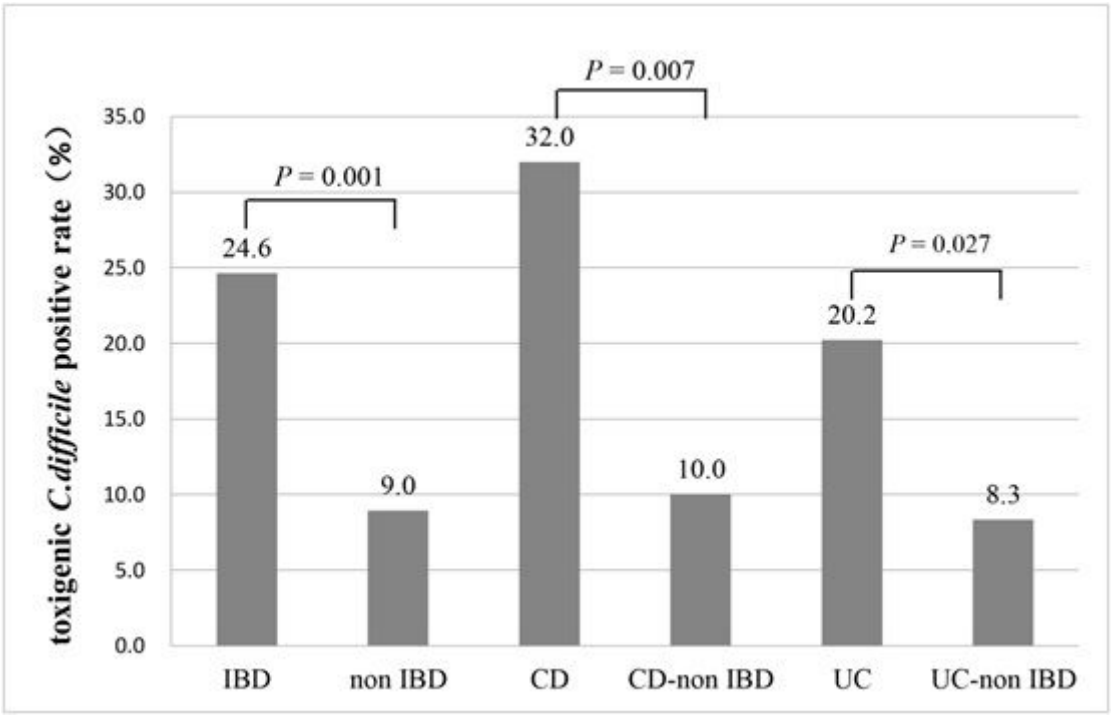

Figure 5

Detection of CDI in IBD patients and matched non IBD patients

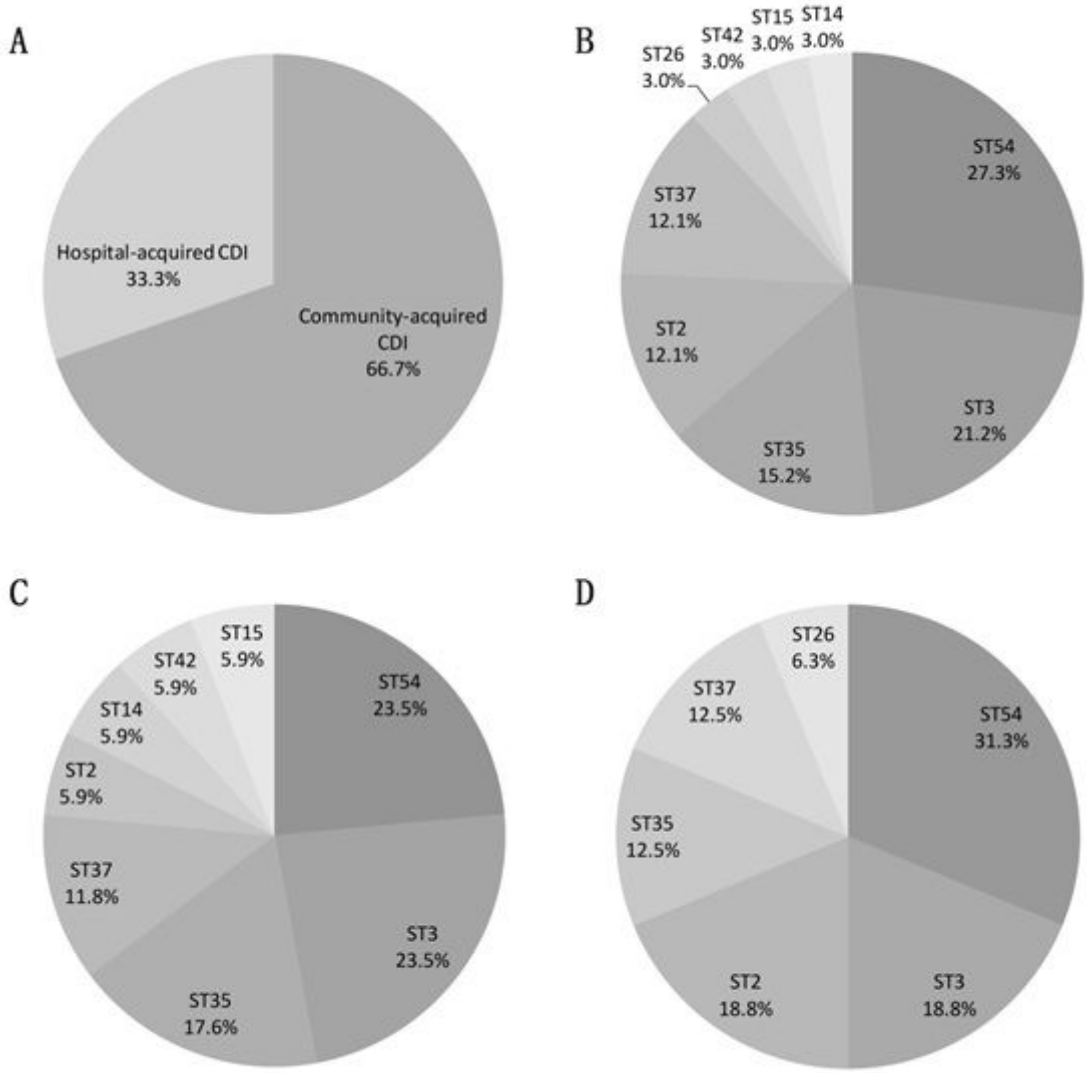

Figure 6

Source and MLST analysis of CDI. A the source of CDI n=33, B MLST of IBD patients n=33, C MLSTof UC patients n=17, D MLST of CD patients n=16