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***Clostridium difficile* Infection in Newly Diagnosed Pediatric Inflammatory Bowel Disease in the Mid-Southern United States**

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Abstract

Clostridium difficile is an emerging opportunistic pathogen that infects patients with underlying chronic disorders such as inflammatory bowel diseases (IBD) at high rates. An extremely high prevalence of *Clostridium difficile* infection (CDI) was noted recently in new-onset pediatric IBD from eastern Europe (Poland). We examined the rate of CDI in our new pediatric IBD patients (123 tested) from 2010 to 2012. The overall prevalence of CDI at disease onset was 8.1%, significantly ($P < 0.0001$) lower than in Poland, but much higher than in the general population. This work supports the testing for *Clostridium difficile* in suspected cases of new-onset pediatric IBD.

Keywords

children; *Clostridium difficile*; incidence; inflammatory bowel disease; pediatric

Clostridium difficile is a Gram-positive anaerobic bacterium responsible for pseudomembranous colitis and is the major cause of antibiotic-associated diarrhea. There has been a drastic increase in *C difficile* infection (CDI) during the last decade in the United States (1,2). This holds true for pediatric CDI as well (3,4), in which relapses are as common as in adults (5).

Inflammatory bowel diseases (IBD) predispose to the development of pediatric CDI (6). The extent of this predisposition may vary depending on geographic location (7). The annualized incidence rate of CDI in patients with IBD from the northern United States was 7.2% between 2007 and 2008 (8). Significantly higher rates of CDI were noted in Polish pediatric outpatients, with a prevalence of 60% (9). Similarly, high prevalence (47%) of CDI was documented by the same group in newly diagnosed pediatric patients with IBD (10). To our knowledge, the incidence and prevalence of CDI in newly diagnosed pediatric patients with IBD within the United States have not been examined. Therefore, we set out to study our patient population in this respect.

METHODS

New-onset patients with IBD were identified through the Baylor College of Medicine institutional review board–approved protocol “Using Patient Data to Transform Care and

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Improve Outcomes for Children With Inflammatory Bowel Disease” (protocol number H-26423) between January 1, 2010 and December 31, 2012. The diagnosis of Crohn disease (CD), IBD unclassified (IBDU), or ulcerative colitis (UC) was established based on clinical signs and symptoms, laboratory parameters, radiologic results, and endoscopic/histologic features. Only the age and diagnosis of the patients were recorded for the purpose of this publication in addition to the information about testing for *C difficile* and outcomes of the test. Testing for *C difficile* was performed from stool specimens with either enzyme immunoassay (EIA, 19/124 cases; 15.3%) or polymerase chain reaction (PCR, 84.7%). Stool test for *C difficile* within 2 months of endoscopic diagnosis was associated with the new diagnoses. Antibiotic exposure before testing was extracted from the charts. This arbitrary cutoff was based upon studies using an 8-week margin for relapse as opposed to new infection (5). Recent work has shown that recurrent episodes of CDI within 1 month are the result of relapse in 76.7% of the cases as opposed to reinfection with a different isolate (23.3%) (11). Guidelines from the Infectious Diseases Society of America suggest a 12-week (~3 months) cutoff to differentiate between relapse and reinfection in adults (12). Hence, the 2-month cutoff (median between 1 month and 3 months) was used. Two-tailed Fisher exact test and unpaired Student *t* test (age) were used to compare individual subgroups. Statistical significance was drawn at $P < 0.05$.

RESULTS

Ten cases (8.1%) were positive for *C difficile* of the 123 tested. Only 42.4% of the total of 290 new IBD cases had documented testing for *C difficile* around the time of diagnosis. The reason for obtaining the test as opposed to not was unclear from the documentation available. The average age of the patients tested was 12.4 years (0.4–19 years), which was similar to those who tested positive (11.6 years [8–18 years], $P = 0.54$), although the age range was less broad in the latter group. There were 54 patients with CD, 18 with IBDU, and 51 with UC. The prevalence of CDI did not differ among these diagnoses (9.3% for CD, 11.1% for IBDU, and 5.6% for UC; $P > 0.5$ for all comparisons). The annualized incidence rate for CDI in new-onset pediatric IBD was 10.2%, 10.5%, and 4.3% in 2010, 2011, and 2012, respectively. The incidence rates among the years examined were not statistically different ($P > 0.2$ in all comparisons). The testing modality for *C difficile* (EIA vs PCR against toxin A and/or B) did not influence the results significantly (5% positive vs 8.7% positive, respectively; $P = 1$). Antibiotic exposure before testing was documented in 7 (70%) of the cases. There was no antibiotic exposure based on history in 1 (10%) proband. Antibiotic use was not commented on in 2 (20%) of the positive cases. The antibiotics used before the diagnosis of IBD complicated by CDI were cephalosporins (3 cases, 1 of which was in combination with azithromycin), nitazoxanide, metronidazole, and trimethoprim/sulfamethoxazole (2 cases). Twenty of the 113 *C difficile*-negative patients with IBD at the time of diagnosis (17.7%) had documentation of previous antibiotic use. Consequently, CDI was associated with a significantly higher exposure to antibiotics (70% vs 18.6% in the *C difficile*-negative group; $P < 0.001$) in the IBD cohort of this report.

DISCUSSION

The overall prevalence of CDI in our new-onset IBD patients (8.1%) in the mid-southern United States is significantly ($P < 0.0001$) lower than in Poland (47% (10)). Interestingly, contrary to our observations, the latter study did not detect an increased exposure to antibiotics in CDI-positive pediatric patients with IBD compared with the CDI-negative ones. The prevalence of CDI without obvious preceding antibiotic exposure was 2.4% in our population. In the meantime, the overall prevalence rate of new-onset IBD-associated CDI in our center is 352-fold higher (odds ratio 384.7 [95% confidence interval 179–826.7]) than the prevalence of CDI in the general pediatric population (without other underlying causes

of diarrhea) of Olmstead County, Minnesota (prevalence 0.023% between 2004 and 2009 (4)). Antibiotic exposure was similar among our CDI-positive patients, and the study group of Olmstead County (70% vs 60.9%; $P = 0.74$). This similarity indicates that the highly increased prevalence of CDI in new-onset pediatric IBD compared with the general population is independent from antibiotic exposure. Age, disease subtype, and mode of testing (EIA vs PCR) did not significantly influence these results. It should be noted that CDI was not detected in 57 new-onset hospitalized cases of pediatric UC in England according to a recent study (13). This result supports our conclusion that geographic variation (among countries and continents) may significantly influence the incidence of CDI in new-onset IBD. Nevertheless, the present work supports the testing for *C difficile* in suspected cases of new-onset pediatric IBD.

REFERENCES

1. Ananthakrishnan AN. Clostridium difficile infection: epidemiology, risk factors and management. *Nat Rev Gastroenterol Hepatol*. 2011; 8:17–26. [PubMed: 21119612]
2. Peery AF, Dellon ES, Lund J, et al. Burden of gastrointestinal disease in the United States: 2012 update. *Gastroenterology*. 2012; 143:1179–1187. e1–e3. [PubMed: 22885331]
3. Kim J, Smathers SA, Prasad P, et al. Epidemiological features of Clostridium difficile-associated disease among inpatients at children's hospitals in the United States, 2001–2006. *Pediatrics*. 2008; 122:1266–1270. [PubMed: 19047244]
4. Khanna S, Baddour LM, Huskins WC, et al. The epidemiology of clostridium difficile infection in children: a population-based study. *Clin Infect Dis*. 2013; 56:1401–1406. [PubMed: 23408679]
5. Kim J, Shaklee JF, Smathers S, et al. Risk factors and outcomes associated with severe clostridium difficile infection in children. *Pediatr Infect Dis J*. 2012; 31:134–138. [PubMed: 22031485]
6. Nylund CM, Goudie A, Garza JM, et al. Clostridium difficile infection in hospitalized children in the United States. *Arch Pediatr Adolesc Med*. 2011; 165:451–457. [PubMed: 21199971]
7. Hojsak I, Ferenc T, Bojanic K, et al. Incidence of Clostridium difficile infection in children with inflammatory bowel disease compared to oncology and immunocompetent patients. *Digestion*. 2012; 86:6–11. [PubMed: 22688504]
8. Mezoff E, Mann EA, Hart KW, et al. Clostridium difficile infection and treatment in the pediatric inflammatory bowel disease population. *J Pediatr Gastroenterol Nutr*. 2011; 52:437–441. [PubMed: 21407116]
9. Wultanska D, Banaszkiewicz A, Radzikowski A, et al. Clostridium difficile infection in Polish pediatric outpatients with inflammatory bowel disease. *Eur J Clin Microbiol Infect Dis*. 2010; 29:1265–1270. [PubMed: 20577773]
10. Banaszkiewicz A, Kowalska-Duplaga K, Pytrus T, et al. Clostridium difficile infection in newly diagnosed pediatric patients with inflammatory bowel disease: prevalence and risk factors. *Inflamm Bowel Dis*. 2012; 18:844–848. [PubMed: 21936029]
11. Figueroa I, Johnson S, Sambol SP, et al. Relapse versus reinfection: recurrent Clostridium difficile infection following treatment with fidaxomicin or vancomycin. *Clin Infect Dis*. 2012; 55(Suppl 2):S104–S109. [PubMed: 22752857]
12. Cohen SH, Gerding DN, Johnson S, et al. Clinical practice guidelines for Clostridium difficile infection in adults: 2010 update by the society for healthcare epidemiology of America (SHEA) and the infectious diseases society of America (IDSA). *Infect Control Hosp Epidemiol*. 2010; 31:431–455. [PubMed: 20307191]
13. Russell RK, Protheroe A, Roughton M, et al. Contemporary outcomes for ulcerative colitis inpatients admitted to pediatric hospitals in the United Kingdom. *Inflamm Bowel Dis*. 2013; 19:1434–1440. [PubMed: 23624885]