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Alimentary Tract

Prevalence and risk factors of *Clostridium difficile* infection in patients hospitalized for flare of inflammatory bowel disease: A retrospective assessment

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ABSTRACT

Background: Recent studies have identified a high frequency of *Clostridium difficile* infections in patients with active inflammatory bowel disease.
Aims: To retrospectively assess the determinants and results of *Clostridium difficile* testing upon the admission of patients hospitalized with active inflammatory bowel disease in a tertiary care centre and to determine the predicting factors of *Clostridium difficile* infections.
Methods: We reviewed all admissions from January 2008 and December 2010 for inflammatory bowel disease flare-ups. A toxigenic culture and a stool cytotoxicity assay were performed for all patients tested for *Clostridium difficile*.
Results: Out of 813 consecutive stays, *Clostridium difficile* diagnostic assays have been performed in 59% of inpatients. The independent predictive factors for the testing were IBD (ulcerative colitis: OR 2.0, 95% CI 1.5–2.9; $p < 0.0001$) and colonic involvement at admission (OR 2.2, 95% CI 1.5–3.1, $p < 0.0001$). *Clostridium difficile* infection was present in 7.0% of the inpatients who underwent testing. In a multivariate analysis, the only independent predictor was the intake of nonsteroidal anti-inflammatory drugs within the two months before admission (OR 3.8, 95% CI 1.2–12.3; $p = 0.02$).
Conclusions: Clostridium difficile infection is frequently associated with active inflammatory bowel disease. Our study suggests that a recent intake of nonsteroidal anti-inflammatory drugs is a risk factor for inflammatory bowel disease -associated *Clostridium difficile* infection.

1. Introduction

Clostridium difficile (*C. difficile*) is a Gram-positive anaerobic spore-forming bacterium that produces toxins. It is responsible for a spectrum of clinical presentations, ranging from asymptomatic carriage to clinically significant diarrhoea, fulminant colitis, sepsis and death [1,2]. Risk factors for *C. difficile* infections (CDI) traditionally include antibiotic use, age, severe comorbidities or contact with healthcare facilities. An alarming trend of increased incidence and severity of CDI over the past several years has been reported worldwide, along with an increased duration of hospitalization and costs [3,4]. As an example, the estimated costs attributed to CDI alone are approximately 3.2 billion dollars per year in the United States [5].

It is particularly difficult to diagnose CDI in patients with inflammatory bowel disease (IBD; Crohn's disease (CD), ulcerative colitis (UC)), because the presentation is similar and consists of abdominal pain and diarrhoea. Indeed, CDI can mimic a flare of the disease, but can also trigger a relapse that could evolve on its own, regardless of the treatment of the infection [6,7]. The relationship between CDI and IBD flares has been recognized as an emerging problem. Several retrospective studies on large populations have suggested a rise in the rate of CDI among patients with IBD along with an increase in disease severity. For example, the incidence of CDI among hospitalized patients with IBD increased from 1.8% in 2004 to 4.6% in 2005 [8]. CDI appeared to be three times more frequent in patients with UC than in patients with CD, but the percentage of patients who were tested for *C. difficile* was not specified [9–12]. CDI was associated with an increased severity of relapse, an increase in the number and length of hospital stays, higher rates of colectomy, and

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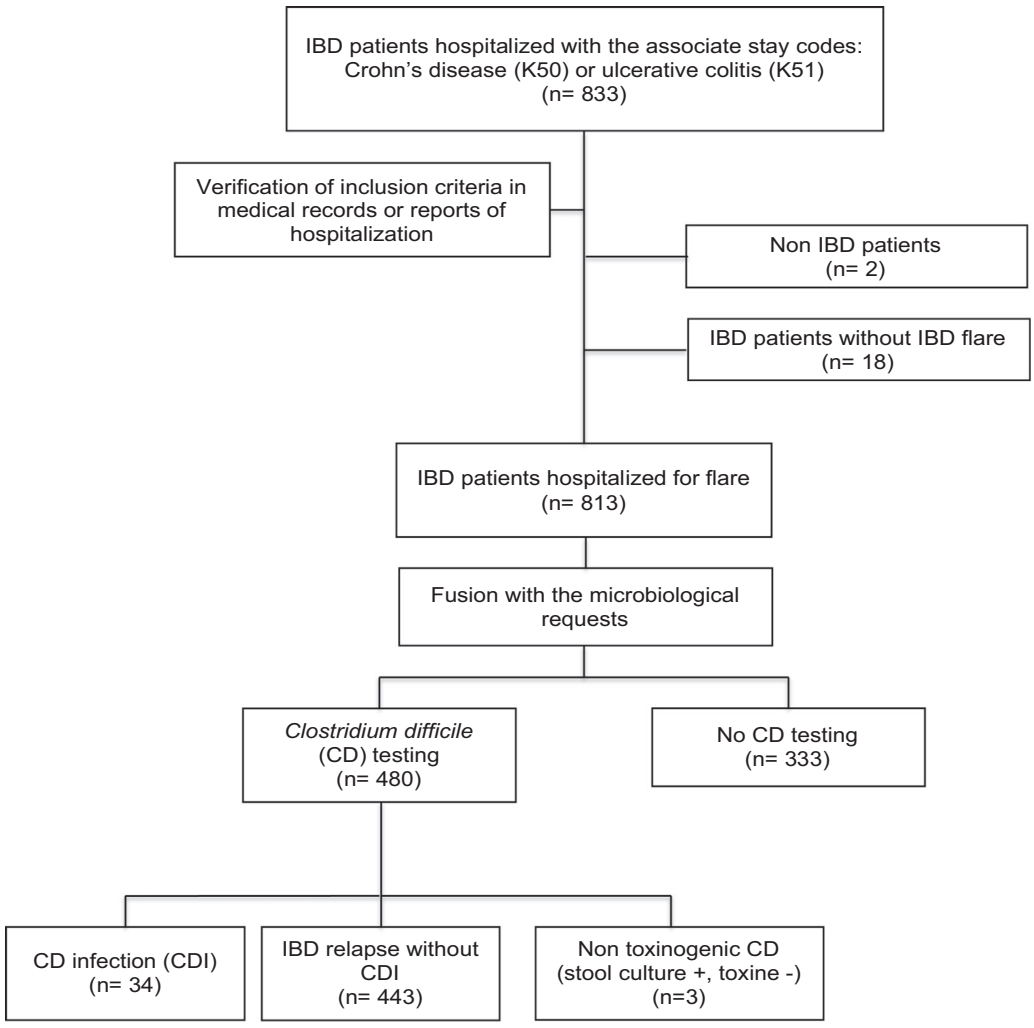

Fig. 1. Flow chart of case definitions in all hospitalized patients for inflammatory bowel disease flares from 2008 to 2010. IBD, inflammatory bowel disease; CD, *Clostridium difficile*; CDI, clostridium *difficile* infection.

a four-fold increase in mortality [9,10]. In these studies, infection in patients with IBD was predominantly community-acquired, in contrast to the general inpatient population where CDI is primarily acquired within the healthcare setting itself [8,12].

To date, the risk factors for CDI in patients with IBD are not firmly established. Some authors have tried to identify them in cohorts that may not necessarily be representative of the study population because they have included all hospitalized patients, whereas they should have included only patients who were tested for *C. difficile*. In our tertiary center, *C. difficile* testing upon the admission of a patient for an IBD flare has been gradually introduced as a routine procedure. This allowed us to conduct this study with two objectives: first, to assess the frequency and the determinants of *C. difficile* testing upon the admission of patients hospitalized for a flare of IBD, and second, to identify risk factors for CDI in patients hospitalized for a flare of IBD.

2. Methods

2.1. Study population and variables

Our study population consisted of all patients hospitalized for IBD flares in the Gastroenterology Department of the Saint-Antoine IBD center from 1 January 2008 to 31 December 2010. We used data from the department of medical information and established a list of all the consecutive stays with the following WHO codes: K 50 (CD) and K 51 (UC). In parallel, using hospitalization reports, we identified all patients with an established diagnosis of IBD and symptoms of active IBD (diarrhoea with possible presence of blood/mucus and/or abdominal cramps) and who were tested for *C. difficile* between 1 January 2008 and 31 December 2010. Those two lists were merged to identify patients who were both hospitalized with a flare of IBD and tested for *C. difficile*. A systematic verification of inclusion criteria was made from reports of hospitalization and/or from medical records. Patients without active IBD at admission were excluded (Fig. 1).

Demographic characteristics included gender, age and body mass index (BMI) classified into three groups (BMI <18.5: underweight, BMI between 18.5 and 25: normal weight, BMI >25: overweight and obesity). Comorbidity was adjusted using the Charlson index, a well-validated mortality prognosis index [13]. Other considered risk factors were current smoking status at admission, history of appendectomy or ICD. Medication use included chronic use of proton pump inhibitors (PPIs), anti-inflammatory drugs (NSAIDs) or antibiotics within the two months prior to hospitalization. We recorded disease characteristics including the type of IBD (i.e., CD or UC), anatomic distribution of the disease (isolated small bowel vs. colonic involvement < or >50%, perianal lesions), the duration of disease from diagnosis and any history of a previous surgical resection (segmental or total colectomy, ileocecal resection). We also recorded the type of therapy, including corticosteroid use within the two months prior to hospitalization, which