# The Management of *Clostridium difficile*-associated Diarrhoea in a Community Hospital

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***ABSTRACT***

***Objective:*** *To review the management of patients with* Clostridium difficile*-associated diarrhoea (CDAD).*

***Methods:*** *A retrospective study was conducted on 26 patients with clinical symptoms of CDAD and positive tests for* C difficile *toxins A and/or B in stool samples, over a 12- month period. Demographic and clinical data on the patients including use of proton pump inhibitors (PPI), management of CDAD, and compliance with local Infection Prevention and Control Guidelines were examined.*

***Results:*** *The majority of patients were over 45 years of age (24/26, 92.4%) and 42% (11/26) were over 80 years of age. At least 50% (13/26) of the patients had acquired CDAD in hospital, 15% (4/26) were community acquired and symptomatic at admission while the onset of diarrhoea following admission to hospital was not documented in 35% (9/26).*

*Three (11%) patients had used PPI. Fifteen per cent (4/26) of patients had no history of previous antibiotic therapy; 40% (10/26) were treated with a cephalosporin, fluoroquinolone or a combination of at least two different classes of antibiotics; one (3%) patient was on augmentin and the antibiotic regime used was not documented in 42% (11/26) who also had previous antibiotic therapy. The conditions for which antibiotics were prescribed could not be ascertained in 58% (15/26) but among the remaining cases antibiotics had been prescribed for urinary tract infection, wound respiratory tract infections and sepsis. Metronidazole (18/26, 70%) was the preferred drug of choice for first line therapy in patients with CDAD. None of the patients in the study received the recommended 10 to 14 days of antimicrobial therapy for CDAD. Recurrent CDAD was observed in 40% of those who were treated with metronidazole. The study also showed that there was timely reporting of laboratory results and good compliance with the hospital Infection Prevention and Control Guidelines.*

***Conclusion:*** *The findings of this study can be used as a process improvement measure in the management of patients with CDAD.*

**Key words:** Antimicrobial therapy, *clostridium difficile*, proton pump inhibitors.

# Tratamiento de Diarreas Asociadas con *Clostridium difficile* en un Hospital Comunitario

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***RESUMEN***

***Objetivo:*** *Revisar el tratamiento de pacientes con diarrea asociada con* Clostridium difficile *(DACD).*

***Método:*** *Se llevó a cabo un estudio retrospectivo de 26 pacientes aquejados por síntomas clínicos de DACD. Dichos pacientes resultaron positivos a pruebas de detección de toxinas A y/o B de* C difficile *en muestras de heces fecales por un período de 12 meses. Se examinaron los datos demográficos y clínicos de los pacientes, incluyendo el uso de inhibidores de la bomba de protones (IBP), tratamiento de la DACD, y el cumplimiento con las guías para el control de la infección local.*

***Resultados:*** *La mayoría de los pacientes tenían más de 45 años de edad (24/26, 92.4%) y 42% (11/26) estaban por encima de los 80 años de edad. Al menos 50% (13/26) de los pacientes habían adquirido*

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*DACD en el hospital; el 15 % (4/26) la adquirió en la comunidad y presentaba síntomas al momento del ingreso; el comienzo de la diarrea tras el ingreso al hospital no se documentó en 35% (9/26) de los casos. Tres pacientes (11%) habían usado IBP. El 15% (4/26) de los pacientes no tenían antecedente alguno de terapia con antibióticos; un 40% (10/26) fue tratado con cefalosporina, fluoroquinolona, o una combinación por lo menos dos clases diferentes del antibióticos; un paciente (3%) se hallaba bajo tratamiento con augmentina y el régimen antibiótico usado no se documentó en el 42% (11/26) de los casos, que también tuvieron terapia antibiótica previa. No pudieron determinarse las condiciones para las que se prescribieron los antibióticos en el 58% (15/26), pero entre los casos restantes, se habían prescrito antibióticos para la infección de las vías urinarias, heridas, infecciones de las vías respiratorias, y sepsis. El metronidazol (18/26, 70%) fue el medicamento de opción preferida para la terapia de primera línea en los pacientes con DACD. Ninguno de los pacientes en el estudio recibió los 10 a 14 días de terapia antimicrobiana, recomendados para la DACD. Se observó DACD recurrente en 40% de aquéllos que fueron tratados con metronidazol. El estudio también mostró que hubo reportes oportunos de resultados de laboratorio y buen cumplimiento de las guías hospitalarias para el control de las infecciones.*

***Conclusión:*** *Los hallazgos de este estudio pueden usarse como medida para mejorar el proceso encaminado a tratar a los pacientes con DACD.*

**Palabras claves:** Terapia antimicrobiana, *Clostridium difficile*, inhibidores de la bomba de protones

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## INTRODUCTION

*Clostridium difficile (C difficile)* is an anaerobic, Gram-positive bacillus which is found in the gastrointestinal tract. *Clostridium difficile* infection causes a spectrum of disease ranging from antibiotic-associated diarrhoea to life-threatening clinical conditions such as pseudomenbranous colitis and severe complications including sepsis syndrome and megacolon (1, 2). It has been well established that *Clostridium difficile* is responsible for 15–20% of antibiotic-associated cases of diarrhoea (1). Initially, it was suggested that *Clostridium difficile*-associated diarrhoea (CDAD) occurred more frequently in the elderly, particularly in people aged 65 years and over. However, recent studies have reported cases of severe disease in young healthy adults and children in the community and outbreaks have been reported in North America and Europe (2–4). The use of broad-spectrum antibiotics is considered the most common predisposing factor for developing CDAD (5). In addition to antibiotic therapy, there have been reports of an association between acid suppression therapy such as proton pump inhibitors (PPIs) and increased risk of *C difficile* infection (6, 7). Gastric acid plays a role in eliminating ingested bacteria from the gastrointestinal tract and it has been suggested that raising the pH of the stomach with acid suppressive therapy may result in increased risk of enteric infections such as CDAD (8–10). The emergence of a hypervirulent fluoroquinolone resistant epidemic strain of *C difficile* has been associated with the changing epidemiology and severity of disease (2, 10). This paper reviews the management of *C difficile* associated diarrhoea at a Bermudian Hospital over a one-year period.

## SUBJECTS AND METHODS

The study involved patients diagnosed with CDAD at the King Edward VII Memorial Hospital, a 250-bed hospital, over the 12-month period January – December, 2008. Cases of CDAD were diagnosed in patients having a liquid stool and a positive *C difficile* toxin A/B test (Wampole C Diff toxin A/B Quik Chek, TECHLAB, VA). A case of community acquired CDAD was defined as a case of CDAD with clinical onset before admission to hospital or within 72 hours after hospital admission with a negative history of hospitalization in the previous 12 weeks (7, 11). Data were collected on the demographic and clinical features of patients with the infection, the use of antibiotics and proton pump inhibitors (PPI), notification of positive results, the management of CDAD and compliance with the hospital's Infection Prevention and Control Guidelines. The data were obtained by reviewing the patients' hospital records.

## RESULTS

During the period of study, 26 patients (16 males and 10 females) were diagnosed with CDAD. The majority (24/26, 92.3%) of the patients were over 45 years of age and 42% (11/26) were over 80 years of age. The majority of patients (19/26) 70.0% were admitted from home. Four patients (15%) were symptomatic at admission, 13 patients (50%) acquired CDAD in hospital whereas there was no documentation on the onset of diarrhoea, in the remaining 9 patients (35%) following admission to hospital. Of 13 cases, classified as hospital acquired CDAD, the onset of diarrhoea was 15 days post admission in 9 (70%) patients and within 10 days of admission in 4 (30%) patients.

It was noted that 4 (15%) patients had no history of previous antibiotic therapy; 40% (10/26) of patients were treated with a cephalosporin, fluorquinolone or a combination of at least two different classes of antibiotics and one (3%) patient with augmentin, while the remaining 42% (11/26) had received antibiotics but there was no documentation of the antibiotic used.

The conditions for which antibiotics had been prescribed included urinary tract infection (4/26, 15%), wound infection (4/26, 15%), sepsis (2/26, 8.0%) and respiratory tract infection (1/26, 4.0%). There was no documentation of the indication for prescribing antibiotics in the remaining 58% (15/26) of patients with CDAD.

In 18 (70.0%) cases, the physician was notified of positive tests for *C difficile* toxin within 48 hours and in six cases (23%) notification was done in less than 24 hours. The remaining two cases (7%) had notification of positive results after 48 hours.

Metronidazole was the first line antibiotic therapy in the majority of patients with CDAD (18/26, 70%) and the antibiotic given was not recorded in the remaining patients. However, none of the patients was given the recommended 14-day course of metronidazole. Of the affected patients, 50% responded well to antimicrobial therapy with metronidazole, as indicated by having a formed stool, while 40% had recurrent CDAD and 10% had loose stool but there was no documentation of the cause or management of these patients with loose stools.

Only 12% (3/26) of patients had used a proton pump inhibitor before the onset of diarrhoea. The majority, 88% (23/26) had not taken proton pump inhibitors prior to the onset of diarrhoea.

Compliance with the hospital Infection Prevention and Control Guidelines was high, greater than 80%, for the majority of cases.

## DISCUSSION

It has been well established that a principal risk factor for CDAD is prior use of broad–spectrum antimicrobial therapy such as fluroquinolones and cephalosporins (5, 7, 10). It is also generally accepted that the judicious use of antibiotics play a pivotal role in *C difficile acquisition* and there have been several reports of successful control of *C difficile* by restriction of broad-spectrum antibiotics in favour of narrow-spectrum antibiotics (12). In the present study, several patients had received broad spectrum antibiotics prior to developing *C difficile* diarrhoea. At least 15% of CDAD cases in this study appeared to be community acquired which is compatible with recent reports of severe disease in adults and children in the community (2–4). However, the proportions of hospital and community acquired cases of CDAD in the study were not precisely determined as acquisition was unclassified in 35% of cases due to incomplete documentation of the onset of diarrhoea.

The recommended treatment for CDAD is metronidazole, 500 mg orally three or four times daily for 10–14 days or vancomycin 125–500 mg orally four times daily for 10–14 days (1, 13). Metronidazole is an inexpensive drug with a greater than 90% positive response rate (14). None of the patients identified in the study received the recommended 10–14 days duration of antimicrobial therapy for CDAD and there was no justification for this approach in the patients' hospital records. Although the majority of patients with CDAD respond well to antimicrobial therapy, recent studies have reported that recurrent disease occurs in 15%–35% of such patients (15, 16). Treatment of recurrent CDAD can be challenging for clinicians. The use of tapered and pulsed regimens of vancomycin, faecal bacteriotherapy, probiotics, prebiotics, intravenous gamma globulin and a *C difficile* toxoid vaccine have been described (15, 16). However, it is well established that *C difficile* infection is due to auto-inoculation or inadequate treatment (16, 17). In practice, another course of antibiotic is administered for 14 days. If this fails, toxin sequestering agents like cholestyramine given 4 hours before vancomycin orally have been used (16–18). The lack of proper antimicrobial management of patients with CDAD at the reporting institution is a concern and will be addressed through education and further audits.

The available data on the patients in this retrospective study were not sufficient to assess the impact of the underlying comorbidities on the source or outcomes of their *C difficile* infection. Several authors have identified risk factors for severe *C difficile* colitis, classification of disease and predictors of mortality (7, 19–20). Recently, Velasquez-Gomez *et al* (7) developed a Severity Score Index, to predict the outcome of a cohort of male patients with *C difficile* infection. This consisted of nine criteria, in the presence of *C difficile* infection, based on literature review and observational experience. Mild disease was classified as having 1–3 criteria, moderate 4–6 and severe disease ≥ 7 criteria. These authors reported that in patients who fulfilled ≥ 7 criteria, mortality was about 75% compared to 4% and 45.5% in those classified as having mild and moderate disease, respectively. The development of fever, tachycardia, leucocytosis or increase in > 10% bands and the presence of colitis seemed to be the most important warning signs and predictors of early mortality in that cohort. The significant risk factors to the development of *C difficile* infection remained the same as in earlier publications, that is, previous use of antibiotics and PPI. In particular, the fourth generation cephalosporins, cefepime and fluoroquinlones demonstrated the strongest association with CDAD. No significant associations were found with feeding tubes, pre-existing co-morbidities or use of histamine-2 blockers (7). Although CDAD occurs most frequently in the older age groups, as was observed in this study, it is of interest to note that age was not among the significant clinical risk factors for mortality, in patients with CDAD, in a number of recent studies (2–4, 7, 19, 20).

At least three cases in the present study had documented evidence of PPI use prior to the onset of diarrhoea. A recent study has reported the inappropriate use of PPIs as a widespread hospital practice and the authors concluded that a reduction of unnecessary PPI use may be an additional strategy in reducing the incidence of CDAD (21).

It is important that healthcare institutions have policies in place to support the control of *C difficile* infection such as active surveillance to monitor local rates of infection. The laboratory should provide the results of patient testing for *C difficile* toxin to clinicians, nurses and infection preventionist in a timely manner to ensure proper management of patients and isolation procedures. In this study, healthcare professionals were notified of *C difficile* results in less than 48 hours in most cases and in some cases on the same day of receiving the stool specimen in the laboratory.

The basic infection prevention and control measures for patients with CDAD such as contact precaution, enhanced environmental and equipment cleaning, wearing appropriate protective clothing, including gloves, gowns and proper hand hygiene, using soap and water are well established (17, 22). The present study has highlighted good compliance with local Infection Prevention and Control Guidelines for the management of patients with CDAD.

The limitations of this retrospective study include incomplete hospital records and the small size of the study population. The study also revealed poor documentation regarding patient medication and the duration of therapy. Action will be taken, through ongoing surveillance, education and process improvements which will impact the hospital stay of patients. Although the number of patients identified in the study was small, important, useful information was obtained.

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