A Retrospective Case-Control Study To Identify Risk Factors Associated With Clostridium Difficile Infection In A Teaching Hospital In Saudi Arabia

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Citation

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Abstract

OBJECTIVE. To determine the incidence of, and predisposing risk factors for, *Clostridium difficile* infection (CDI) in Saudi Arabia.

DESIGN. Retrospective case-control study.

SETTING. A tertiary teaching hospital.

PARTICIPANTS. The study involved 183 patients, comprising 61 (33%) CDI and 122 (66%) control cases. The CDI cases included patients with diarrhea and positive enzyme immunosorbent assays (ELISAs), and the control subjects included those with diarrhea and negative ELISAs. The cases:controls ratio was 1:2.

PRIMARY OUTCOME MEASURES. Univariate and multivariate analyses determined the association between CDI and different risk factors.

RESULTS. Men comprised 70% of the CDI cases and the mean age of the cases was 59 (27.2) years. One CDI case (1.6%) relapsed. The CDI annual incidence from 2013 to 2014 was 1.5 per 10,000 patient days and it was 1.7 per 10,000 patient days in 2015. Using proton pump inhibitors (PPIs) ($P < .05$), the presence of inflammatory bowel disease (IBD) ($P = .04$), intestinal obstruction ($P = .01$), and using antibiotics, including ceftriaxone ($P < .05$) and clindamycin ($P < .05$), were independent predictors of the incidence of CDI.

CONCLUSION. The CDI incidence is lower in Saudi Arabia than in North America. Clindamycin and ceftriaxone use, PPI use, and the presence of an intestinal obstruction or IBD are independent risk factors for the incidence of CDI in Saudi Arabia. Further studies are required to determine the CDI prevalence in Saudi Arabia, the relapse rate, and the risk factors.

Strengths and limitations of this study

- The strengths of this study include its retrospective design, its setting in a teaching hospital, and its 3-year duration.
- The univariate and multivariate analyses strengthened the evidence.
- The diagnosis of our cases was based on toxin identification and the clinical symptoms that characterize Clostridium difficile infection.
- We did not include some parameters, namely, the duration of hospital stay and the duration of antibiotic administration.
- We did not evaluate the CDI cases and the control cases in relation to the departments in which they had undergone treatment.

INTRODUCTION

Clostridium difficile infection (CDI) is a common cause of antibiotic-associated diarrhea in healthcare settings.1 Since the turn of the century, increases in the incidence, severity, and relapse rate of CDI have elevated the disease's economic burden and they have reduced hospital safety.2-5 The emergence of virulent and drug-resistant *C. difficile* strains is exacerbating the situation.6 The changing epidemiological and etiological scenarios and the Quebec outbreak have generated concern and interest in the epidemiology, prevention, and treatment of *C. difficile*-related conditions.7 The presentation of CDI varies widely, with patients ranging from being asymptomatic to displaying episodes of diarrhea or colitis or other complications that can be fatal.4 CDI increases mortality rates, the duration of hospital stay, and healthcare costs, thus leading to significant burdens on healthcare systems.8 However, little epidemiological data describing CDI in Saudi Arabia are available.9 Al Tawfiq et al.9 reported annual incidence rates of 1.2 and 0.9 per 1,000 discharges in 2007 and 2008, respectively, and 2.4 and 1.7 per 10,000 patient days in 2007 and 2008, respectively, in Saudi Arabia. These rates are low compared with westernized countries, but the data are insufficient to enable an evaluation of, or to facilitate improvements in, healthcare infection control systems.

When determining the incidence rates of new cases and the recurrence rates of CDI in hospital settings, it is vital to understand the risk factors associated with the incidence of CDI. Antimicrobial therapy is the most recognized modifiable risk factor, yet different classes of antimicrobial therapy pose different levels of risk.10 Furthermore, the association between the use of proton-pump inhibitors (PPIs) and the incidence of CDI is being continuously evaluated.11-13 Other risk factors, including increasing age, prolonged hospital stays, immunosuppression, chronic kidney disease (CKD), and the presence of inflammatory bowel disease (IBD), have also shown direct relationships with CDI.1,14-16 The huge CDI burden among elderly people might be compounded by the use of multiple medications for their comorbidities.1,17 Although these risk factors have been comprehensively investigated in westernized countries, it is extremely important to generate data from local studies to guide hospital antibiotic policies. Thus, the odds of the incidence of CDI in relation to the known or new risk factors in the context of the Saudi Arabian healthcare system must be determined. While ascertaining the roles of the risk factors, we must be able to fully understand our infection control systems, because the Quebec outbreak was mainly attributed to deficient infection control systems.18

This study aimed to estimate the incidence of CDI and to identify the risk factors associated with CDI at a teaching hospital in Saudi Arabia. To the best of our knowledge, this is the first case-control study from Saudi Arabia that identifies the risk factors associated with CDI.

METHODS

This was a case-control study that involved patients who were admitted to a tertiary care teaching hospital between January 2013 and December 2015. The hospital has 860 beds and it is affiliated to medical and nursing schools. The hospital admits 35,685 patients per year on average and specializes in different medical disciplines. It provides services to a large proportion of the community.

We identified the CDI cases as those patients who had been admitted to the hospital for at least 48 h, had diarrhea, and had tested positive for C. difficile toxin A or B using an enzyme immunoassay. The control cases defined those patients who had been admitted to the same hospital for at least 48 h, had diarrhea after use of antibiotic, and had shown 2 or 3 negative results for CDI using an enzyme immunoassay. All patients within the departments of medicine, surgery, and obstetrics and gynecology were included in the analysis. Pediatric patients and those who had community-acquired CDI, which was defined as a CDI that was acquired before admission or within less than 48 h of being admitted, were excluded from the study. The ratio of CDI cases to control cases was 1:2. Ethical approval for the study was provided by the institutional review board.

The patients' information was collected from their hospital records. Demographic and clinical data, including the patients' names, ages, genders, diagnosis upon admission, the dates of the patients' previous admissions to the hospital, the lengths of the hospital stay, and the use of antibiotics and PPIs during admission and during the 12 weeks before admission, were recorded. The data were stored using patient identifiers rather than the patients' names.

The sample size was calculated in EPI INFO program Two-sided confidence level 95% ratio of case to control 1:2 power of the study80%

Data analysis

The analysis was carried out to identify how different values

of independent variables may impact our dependent variable. Afterwards, we can adjust for those variables in our regression models. Chi square test was used for categorical variables, while continuous variables associations were examined using t-test (age and length of hospital stay). Subsequently, significant association between measured variables and outcome was examined using univariate logistic regression for cases and controls at a significance level of 0.05. Finally after variables with significant associations with outcome were identified, a multivariate logistic regression model was used to identify independent variables associated with CDI and to calculate odds ratio with 95% confidence intervals.

RESULTS

Incidence of C. difficile Infection and the Patients' Characteristics

From January 1, 2013 to December 31, 2015, 47,695 patients were admitted to King Abdulaziz University Hospital, and, of these, 183 patients were included in the study, comprising 61 (33%) CDI cases, and 122 (67%) control cases. Most (70%) of the CDI cases were men, and there was no difference in relation to the gender distribution among the control cases. The mean (SD) ages of the CDI cases (52 [24] years) and the control cases (51 [20] years) were similar (P = .002). The incidence of CDI was 1.7 per 10,000 patient days in 2015 and 1.5 per 10,000 patient days in the year from 2013 to 2014. One CDI case (2%) relapsed. Table 1 shows the demographic and clinical details of the patients who were included in this study.

In Multivariant analysis model could be delicate in some instances due to intercorrelation between covariates in one single model. Table 3 shows that is included variables that did not have any significant association with CDI in the univariate logistic regression. Moreover, the variable "hospital admission in the previous 6 weeks "did not show significance in multivariant logistic regression model although it was significant in its univariate model.

Comorbid Conditions

There was significant difference between the percentage of the CDI cases (70%) and the percentage of the control cases (47%) that was highly associated with a higher incidence of CDI among males (P ≤ .002). Also there was a significant difference between the mean age of CDI cases and controls (OR, 3; 95% CI, 48–54.5; P ≤ .005). Furthermore, the mean length of hospital stay showed a significant association between CDI cases and control cases (OR, 2; 95% CI, 38.7–54.2; P ≤ .001). In, addition, a significantly higher percentage of the CDI cases had undergone abdominal surgery (20%) compared with the control cases (4%) (P ≤ .05) (Tables 1 and 2), and undergoing abdominal surgery was significantly associated with a higher incidence of CDI (OR, 7.22; 95% CI, 2.22–23.50; P ≤ .05).

A history of intestinal obstruction was associated with a higher risk of the incidence of CDI (OR, 3.1; 95% CI, 2.48–3.78; P = .04). There were no significant differences between the groups with respect to the prevalence of diabetes mellitus, hypertension, and malignancy. IBD was associated with a higher risk of CDI (OR, 16; 95% CI, 2.8–13.1; P ≤ .05).

Hypertension was more prevalent among the CDI cases (51%) compared with the control cases (43%), but did not show any significance (OR, 1.3; 95% CI,1.2–2.5; P ≤ .21)

Concomitantly Administered Drugs

Table 2 shows the use of antibiotics within the 2 groups. Cases who had been administered piperacillin-tazobactam in combination, amoxicillin-clavulanic acid, cefepime, ciprofloxacin ceftriaxone, or clindamycin had a significantly higher incidence of CDI. There were no significant differences between the groups in relation to the occurrence of CDI among the cases who received other antibiotics, including colistin, cefazolin, ceftazidime, gentamicin, meropenem, and vancomycin.

Risk Factors Associated with the Occurrence of C. difficile Infections

The multivariate analyses of the variables determined that a history of intestinal obstruction, the use of PPIs, ceftriaxone, or clindamycin, and the presence of IBD were risk factors for the occurrence of CDI (Table 3).

DISCUSSION

The findings from this retrospective case-control study show that many patient- and treatment-specific factors are independent predictors of the occurrence of CDI. The independent risk factors associated with the occurrence of CDI included a history of bowel obstruction, the use of PPIs, the presence of IBD, and the use of antibiotics, namely, ceftriaxone and clindamycin. The univariate analyses demonstrated associations between CDI and the use of

piperacillin-tazobactam, amoxicillin-clavulanic acid, cefepime, and ciprofloxacin, in addition to the aforementioned antibiotics.

Evaluating the risk factors for CDI development is critical, because the CDI incidence and recurrence rates have increased significantly. In the USA and Europe, the incidence of recurrent C. difficile (RCDI) associated diarrhea has increased markedly.16,17 Even though the current study was the second epidemiological study that sought to understand the risk factors for CDI in Saudi Arabia, some retrospective and prospective studies carried out in other countries have identified similar risk factors associated with CDI. Our evaluation has similarities and dissimilarities compared with earlier studies. A prospective, observational, hospital-based study undertaken by Al-Tawfiq et al.9 is the only investigation into the epidemiology of CDI in Saudi Arabia that has been undertaken previously. The incidence of CDI in our study was 1.7 per 10,000 patient days in 2015, which is similar to that reported from the earlier study conducted in Saudi Arabia, but it is lower than the incidence rates reported from studies undertaken in westernized countries.19 Hence, further studies are required to determine the reasons underlying these differences. Our results showed a recurrence rate of 3.27%, which is lower than the recurrence rates reported from earlier studies (10%) and meta-analyses (13%–50%).20-22 The mean (SD) ages of the CDI cases and the control cases were 52 (24) years and 51 (20) years, respectively. Similarly, Al-Tawfiq et al. reported a mean (SD) age of 44.6 (27.2) years.9 While increasing age is considered an important risk factor for CDI,20,21 there was no significant difference between the CDI cases and the controls with respect to the age of the patients in the current study. CDI has been reported to be more common among elderly people because of the presence of comorbid conditions, immunosuppression, and the use of multiple drugs. Daniel and Rapose2 undertook a 1-year evaluation of the risk factors associated with CDI among patients in a community-based hospital in the USA and found that most (87%) of the patients were over 60 years of age.

The association between antibiotic use and the incidence of CDI is well-established.23 Antibiotics cause alterations in the normal gut flora that are an important cause of CDI.22 However, variable results have been reported with respect to the odds of CDI developing in association with specific drug groups.4,24,25 Tartof et al.25 recently reported an increased risk of CDI in association with the inpatient use of third-generation cephalosporins, fluoroquinolones (for urinary tract infections), metronidazole, broad-spectrum penicillins, lincosamides, and oral vancomycin. The outpatient use of fluoroquinolones and lincosamide increased the risk of CDI, but none of the other antibiotics had an effect on the incidence of CDI.25 Babey et al.26 also reported associations between the risk of CDI and the use of ciprofloxacin, cephalosporins, and clindamycin from a study of rural hospitals in Ontario, Canada, and these findings are similar to the results from the current study. Al-Tawfiq et al.9 reported that around 39% of their study population had not received any antimicrobial agents during the 3 months before testing. Of those who had been administered antimicrobial agents and had developed CDI, cephalosporins and fluoroquinolones were the most commonly administered antibiotics. Daniel and Rapose2 reported that 74% of their patients had taken antibiotics during the 6 months that preceded their study. Unlike our study, the use of beta-lactam antibiotics either alone or in combination was significantly more common among the patients, and clindamycin was administered to only 4% of the patients. On the other hand, Weiss et al.18 determined that there were no correlations between CDI and the type and the amount of antibiotic used in a hospital setting, and they explained that the outbreak of CDI in Quebec might have been a consequence of improper infection control policies in the state.18

In parallel with the increasing incidence and severity of CDI, the relationship between IBD and CDI has been established.12,13,27 The results from the current study showed that IBD is an independent predictor of CDI. The relationship between IBD and CDI is critically important because of the overlapping clinical presentations that limit correct diagnoses and treatment.12 Other diseases, for example, CKD and liver disease, have also been established as risk factors for CDI.8,13 Chronic inflammation and the acquired immunodeficiency associated with CKD might underlie increases in susceptibility to CDI.28 Our analysis could not establish any associations between comorbid conditions that included diabetes mellitus, hypertension, and any malignancies, and the incidence of CDI. The findings from a community hospital-based retrospective analysis undertaken in the USA showed that the comorbidities among CDI patients included malignancies, diabetes mellitus, and CKD.2 Abdelfatah et al. evaluated the incidence of, and the risk factors for, RCDI in a study of more than 2,000 patients,

and found increased risks of RCDI among patients with CKD (OR, 1.3; 95% CI, 1.0–2.4; P = .039) and among those who used glucocorticoids (OR, 1.65; 95% CI, 1.0–1.5; P = .047).29

The association between PPI use and CDI has been reported internationally,17,18 but some studies' findings have not demonstrated an association between PPI use and CDI.22,25 The recognition of the association between the use of PPIs and the incidence of CDI led the United States Food and Drug Administration to issue warnings about the risk of CDI when PPIs are used.30 Daniel and Rapose reported that more than 50% of their CDI patients were using PPIs when they were admitted to hospital.2 One possible explanation for the increased incidence of CDI may relate to the changes in the stomach's acidity and the normal flora that are caused by PPIs, which may predispose patients to CDI.26 Our results also showed that PPI use was an independent predictor of the incidence of CDI. However, some unanswered questions about the association between CDI and PPI use remain, including the duration of PPI use that is required to increase the incidence of CDI and whether PPI use is related to the rate of CDI recurrence. We did not record the durations of PPI administration in the current retrospective analysis, so we could not determine the significance of the duration of PPI use that was reported by Barletta et al.30 The association between PPI use and the risk of recurrence is currently being evaluated. There are conflicting views about the risk associated with the use of PPIs and the recurrence of CDI.31,322 Abdelfatah et al.29 found an association between the use of PPIs (OR, 1.65; 95% CI, 1.0–1.7; P = .002) and RCDI. It is vital to determine the associations between PPI use and CDI and RCDI.

Other risk factors that have been studied and reported include an increased heart rate, tachypnea, abnormal white blood cell counts of <4 × 109/L (OR, 2.6; 95% CI, 1.3×5.5) and ≥20 × 109/L (OR, 2.2; 95% CI, 1.2–4.0), serum albumin levels of <25 g/L, and C-reactive protein levels of ≥150 mg/L.33

This study has some limitations that are described next. Although we tried to find all of the data to gain an understanding of the risk factors, we did not include some parameters, namely, the durations of the hospital stays and the durations of antibiotic administration, and analyzing these factors could have enhanced the relevance of our results. While we considered the use of specific antibiotic groups as risk factors, the duration of antibiotic use is also very important. Similarly, a long hospital stay is a known risk factor for CDI.4 However, a cut-off time for this risk factor has not been established. Furthermore, we did not evaluate the CDI cases and the control cases in relation to the departments in which they had undergone treatment. Data describing inpatient and outpatient antibiotic use could have generated more robust evidence.

The strengths of our study include its retrospective design, its setting in a teaching hospital, and its 3-year duration. We tried to capture all of the data that were available in the patients' electronic medical records. The univariate and multivariate analyses strengthened the evidence. Additionally, the diagnosis of our cases was based on toxin identification and the clinical symptoms that characterize CDI.

As CDI augments the burden on healthcare systems by increasing mortality, morbidity, hospital stays, the requirement for surgery, and costs, it is extremely important to gain an understanding of the global and local risk factors. Our results are particularly important because there is a dearth of evidence from our country. Our results have strengthened the evidence for the existence of risk factors for CDI in Saudi Arabia that are similar to those that are present elsewhere, and they have simultaneously provided the CDI incidence rate from a teaching hospital in Saudi Arabia. These results are critical for guiding the careful administration of drugs, such as metronidazole and vancomycin, which are effective at treating CDI. Additionally, the results will guide the implementation of suitable measures, including the appropriate use of antimicrobial agents, to reduce the incidence of both hospital- and community-acquired CDI. Such clinical evidence is essential if the morbidity and mortality associated with CDI are to be reduced. Following the evaluation of so many potential risk factors, there is a need to investigate associations with other factors, including the availability of specialized nursing skills, the concomitant use of antimicrobial agents, empirical treatment, and the use of antibiotic stewardship guidelines. Proper care and risk factor evaluations can reduce the incidence and recurrence of CDI. Additionally, the preferred antibiotic combinations can be determined.

In conclusion, the findings from our study demonstrate that the CDI incidence and relapse rates remain low in Saudi Arabia, and that a history of intestinal obstruction, PPI use, the presence of IBD, and the use of antibiotics, for example,

ceftriaxone and clindamycin, are independent predictors of the incidence of CDI. Further studies are needed to confirm and to determine the reasons that underlie these findings.

Limitation of the study

One of the limitations of the study, interpreting detailed significance for antibiotic use may not be possible; this is because the length of use for each antibiotic was not included in this study.

Table 1

Baseline characteristics of the cases infected by Clostridium difficile and the control subjects

Variables	CDI cases (n = 61)	Control cases (n = 122)
Age, years, mean (SD)	52 (24)	51 (20)
Gender		
Male, n (%)	43 (70)	57 (47)
Length of hospital stay, days, mean (SD)	46 (56)	46 (55)
Previous hospital admission within 6 weeks		
Yes, n (%)	34 (56)	61 (50)
No, n (%)	27 (44)	61 (50)
CDI relapse		
Yes, n (%)	3 (5)	0 (0)
No, n (%)	85 (95)	122 (100)
Relevant comorbidities		
Hypertension		
Yes, n (%)	31 (51)	53 (43)
No, n (%)	30 (49)	69 (57)
Diabetes mellitus		
Yes, n (%)	30 (49)	56 (46)
No, n (%)	31 (51)	66 (54)
Malignancy		
Yes, n (%)	15 (25)	30 (26)
No, n (%)	46 (75)	92 (74)
Chronic kidney disease		
Yes, n (%)	37 (60)	77 (63)
No, n (%)	24 (39.3)	45 (37)
Inflammatory bowel disease Yes		
Yes, n (%)	7 (11)	1 (1)
No, n (%)	54 (88)	121 (99)
Abdominal surgery (laparotomy)		
Yes, n (%)	12 (20)	4 (4)
No, n (%)	49 (80)	118 (96)
Intestinal obstruction		
Yes, n (%)	2 (3.3)	0 (0)
No, n (%)	11 (97)	122 (100)

Table 2

Factors associated with adult nosocomial Clostridium difficile infections determined using univariate analyses (SD, standard deviation; CDI, Clostridium difficile infection; IBD, inflammatory bowel disease; NGT, nasogastric tube; PPIs, proton pump inhibitors; TPN, total parenteral nutrition.)

Variable	CDI cases (n = 61)	Control cases (n = 122)	Odds ratio	95% confidence interval	*P* value
Mean (SD) Age, years	52 (24)	51 (20)	3	48–54.5	**≤.005**
Gender					
Male, n (%)	43 (70)	57 (47)	3	1.4–5.4	**.002**
Mean (SD) length of hospital stay, days	46 (56)	46 (55)	2	38.7–54.2	**≤.001**
Hospital admission in the previous 6 weeks					
Yes, n (%)	34 (56)	61 (50)	1.3	1.61–2.34	**≤ .05**
No, n (%)	27 (44)	61 (50)			
Abdominal surgery (laparotomy)					
Yes, n (%)	12 (20)	4 (4)	7.22	2.22–23.50	**≤ .05**
No, n (%)	49 (80)	118 (96)			
Intestinal obstruction					
Yes, n (%)	2 (3.3)	0 (0)	3.1	2.48–3.78	**.04**
No, n (%)	11 (97)	122 (100)			
CDI relapse					
Yes, n (%)	3 (5)	0 (0)	3.03	2.46–61.73	.33
No, n (%)	58 (95)	122 (100)			
TPN					
Yes, n (%)	19 (31)	40 (33)	1	0.49–1.84	.50
No, n (%)	41 (67)	82 (67)			
NGT					
Yes, n (%)	25 (41)	42 (34)	1.3	0.77–2.25	.39
No, n (%)	36 (59)	80 (66)			
Use of PPIs					
Yes, n (%)	53 (87)	60 (49)	7.8	3.29–18.57	**≤ .05**
No, n (%)	8 (13)	62 (51)			
Diabetes mellitus					
Yes, n (%)	30 (49)	56 (46)	0.44	0.54–2.05	.44
No, n (%)	31 (51)	66 (54)			
Chronic kidney disease					
Yes, n (%)	37 (60)	45 (37)	1	0.48–1.60	.1
No, n (%)	24 (39.3)	77 (63)			

Table 2 continued

Hypertension					
Yes, n (%)	31 (51)	53 (43)	1.3	0.73–2.49	.21
No, n (%)	30 (49)	69 (57)			
Malignancy					
Yes, n (%)	15 (25)	30 (26)	1	0.49–1.79	.58
No, n (%)	46 (75)	92 (74)			
IBD					
Yes, n (%)	7 (11)	1 (1)	16	2.81–13.11	≤ .05
No, n (%)	54 (88)	121 (99)			
Piperacillin-tazobactam					
Yes, n (%)	28 (46)	38 (31)	2	1.90–3.51	≤ .05
No, n (%)	33 (54)	84 (69)			
Amoxicillin-clavulanic acid					
Yes, n (%)	7 (11)	0 (0)	3.3	2.61–4.10	≤ .05
No, n (%)	54 (89)	122 (100)			
Ciprofloxacin					
Yes, n (%)	29 (46)	29 (24)	2.90	1.51–5.58	≤ .05
No, n (%)	32 (52)	93 (76)			
Ceftriaxone					
Yes, n (%)	21 (34)	24 (20)	2.14	1.14–2.28	≤ .05
No, n (%)	40 (66)	98 (80)			
Clindamycin					
Yes, n (%)	10 (16)	4 (3)	6	1.73–19.30	≤ .05
No, n (%)	51 (84)	118 (97)			
Colistin					
Yes, n (%)	2 (3)	10 (8)	0.4	0.91–1.79	.17
No, n (%)	59 (97)	112 (92)			

Table 2 continued

Cefazolin					
Yes, n (%)	6 (10)	2 (2)	6.5	1.28–33.46	.54
No, n (%)	55 (90)	120 (98)			
Ceftazidime					
Yes, n (%)	6 (10)	7 (6)	1.7	0.57–5.58	.23
No, n (%)	55 (90)	115 (94)			
Cefepime					
Yes, n (%)	2 (3)	0 (0)	3.2	2.58–3.78	.04
No, n (%)	59 (97)	122 (100)			
Vancomycin					
Yes, n (%)	17 (28)	47 (39)	0.62	0.31–1.20	.10
No, n (%)	44 (72)	75 (61)			
Gentamicin					
Yes, n (%)	11 (2)	14 (12)	1.7	0.72–400	.16
No, n (%)	50 (98)	88 (88)			
Meropenem					
Yes, n (%)	32 (52)	49 (40)	2	1.8–3.1	.07
No, n (%)	29 (48)	73 (60)			

Table 3

Factors associated with adult nosocomial Clostridium difficile infections determined using multivariate analyses

Variable	Odds ratio	95% confidence interval	*P* value
History of abdominal surgery	2	2.57–6.42	.16
Intestinal obstruction	3	2.56–3.78	.01
Chronic kidney disease	1	0.48–1.46	.74
Inflammatory bowel disease	2.60	1.12–5.04	.04
Use of proton pump inhibitors	2.20	3.4–5.98	≤ .05
Piperacillin-tazobactam use	0.51	0.50–1.52	.32
Ciprofloxacin use	0.86	0.12–1.85	.09
Ceftriaxone use	1.04	1.20–2.1	≤ .05
Clindamycin use	2.33	1.56–4.13	≤ .05

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