Epidemiology of Suspected *Clostridium difficile*-Associated Hospital-Acquired Diarrhea in Hospitalized Patients at Siriraj Hospital

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Background: *Clostridium difficile-associated disease (CDAD) is an important cause of hospital-acquired diarrhea.*
Objective: *To determine the prevalence, risk factors, diagnosis, treatments and outcomes of the patients with CDAD in hospitalized patients at Siriraj Hospital.*
Material and Method: *The medical records of hospitalized patients aged older than 14 years who developed hospital-acquired diarrhea and their stool samples were sent for detection of C. difficile toxins from March to June 2008 were reviewed. Risk factors of CDAD were identified by reviewing medical records of CDAD patients (case group) and patients who had hospital-acquired diarrhea without C. difficile toxins (control group). The patients in the control group were matched with the case group in terms of gender and age.*
Results: *Three hundred and twenty three stool samples obtained from 255 adult hospitalized patients were sent to microbiology laboratory for detection of C. difficile toxins. The prevalence of CDAD in suspected C. difficile-associated hospital-acquired diarrhea was 12.3% (95% CI 8.5% to 17.6%). Univariate analysis showed that antibiotic use (≥ 2 agents), proton pump inhibitor (PPI) use, hematologic malignancy, receiving chemotherapy or immunosuppressive agents were associated with CDAD. Multivariate analysis revealed that only antibiotic use (≥ 2 agents), PPI use and hematologic malignancy were independent risk factors associated with CDAD. Nasogastric intubation was observed to be associated with CDAD as a protective factor from both univariate and multivariate analyses. Diagnosis of CDAD in most of the patients was made by a presence of C. difficile toxin in their stool samples. Response rate to metronidazole was 74.5%. The recurrence rate of CDAD was 3.2%. The mortality rate due to CDAD was 3.2%.*
Conclusion: *CDAD is not uncommon in the patients with hospital-acquired diarrhea especially in those who have hematologic malignancy, receive multiple antibiotics or receive PPI. Metronidazole is an acceptable treatment for CDAD. The recurrence rate of CDAD and mortality rate due to CDAD are low.*

Keywords: *Clostrium difficile, Hospital-acquired diarrhea*

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Clostridium difficile-associated disease (CDAD) is an important hospital acquired diarrhea. Clinical manifestations of *C. difficile* infection (CDI) range from mild or moderate diarrhea to life-threatening pseudomembranous colitis (PMC)[1]. CDI is contributed to 15%-25% of all cases of antibiotic associated diarrhea (AAD) and colitis and more than 95% of cases of antibiotic-associated PMC[2]. Since 2001, there have been several outbreaks of CDI in Canada, USA and several countries in Europe with a new virulent strain and possibly resistant strain of *C. difficile* causing more severe disease[3-9]. Major risk factors for CDI include antibiotic exposure, hospitalization and advanced age[10]. The previous study reported the prevalence of *C. difficile* isolated from the stools in Thai adult patients with suspected AAD was 18.6%[11]. A report determining patients' characteristics, treatment and clinical outcomes of CDAD in Thai patients was recently published[12]. However, this study did not determine risk factors of CDAD in Thai patients.

The objectives of the present study were to

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determine the prevalence of CDAD in suspected *C. difficile*-associated hospital acquired diarrhea in hospitalized patients at Siriraj Hospital and to determine risk factors for developing CDAD as well as treatments and outcomes of the patients with CDAD.

Material and Method

The study was cross-sectional and matched case-control study. This study was approved by Institutional Review Board of Siriraj Hospital.

Study patients

All medical records of the patients aged older than 14 years who were hospitalized at Siriraj Hospital and developed nosocomial diarrhea and whose stool samples were sent for detection of *C. difficile* toxin A and B from March to June 2008 were retrieved from the medical record department. Each medical record was reviewed for demographics, clinical features, investigations, diagnosis, treatment and clinical course. *C. difficile* toxin A and B in stool samples were detected by Remel Xpect (rapid immunochromatographic test; Remel, Lenexa, KS, USA). Medical records of the patients with *C. difficile*-associated hospital-acquired diarrhea from January to February and from July to December 2008 were also reviewed. The medical records of the patients who had hospital-acquired diarrhea without CDAD (control group) from January to December 2008 were reviewed in order to determine the risk factors of CDAD. The patients in the control group were matched with CDAD patients according to their gender and age (+/- 5 years). The number of the patients in the control group was twice that of the patients with CDAD.

Definitions

Nosocomial diarrhea is defined as diarrhea which occurred at least 72 hours after hospitalization. *Clostrium difficile*-associated disease is diagnosed by documented diarrhea plus positive laboratory confirmation for *C. difficile* toxin A/B and/or visualization of pseudomembrane of colon on colonoscopy/sigmoidoscopy or pathological diagnosis of CDAD or typical finding of PMC on abdominal CT scan.

Statistical analyses

The data were analysed by descriptive statistics and comparison of the variables between the groups were done by Student's t-test and X^2 test. Odds ratio and 95% CI were calculated according to standard methods. A multivariate logistic regression model was used to assess risk factor for developing CDAD. The variables were selected for factors including in the regression model if such variables were significantly associated with CDAD. A p-value ≤ 0.05 was considered statistically significant.

Results

From March to June 2008, 323 stool samples obtained from 255 adult hospitalized patients were sent to microbiology laboratory for *C. difficile* toxin A/B test. Fifty-two patients were excluded due to community-onset diarrhea (n = 48) and unavailability of medical records (n = 4). Twenty-five patients were diagnosed as CDAD (21 had positive CDT, 2 had PMC on colonoscopy, and another 2 had typical findings of PMC on abdominal CT scan). The prevalence of CDAD in 203 patients suspected *C. difficile*-associated hospital-acquired diarrhea at Siriraj Hospital was 12.3% (95% CI 8.5% to 17.6 %).

Sixty-two patients were diagnosed as having CDAD from January to December 2008. The demographics, clinical features, investigations, diagnosis, treatment and clinical course of 62 cases of CDAD are shown in Table 1. The mean age was 66 years and 52% were females. All patients had diarrhea and 22% had abdominal tenderness. The patients with CDAD usually had multiple comorbidities and the most common comorbidity was hematologic malignancy. Many patients received chemotherapy and antibiotics. Cephalosporins were commonly prescribed in 62.9%. Proton pump inhibitor drugs were given to 88.7% of patients prior to developing CDAD. Most of the patients with CDAD were diagnosed by a presence of *C. difficile* toxin in their stool samples. Seven patients had typical PMC on endoscopy. PMC in most cases were found at rectum and sigmoid colon, except one patient who had the lesion localized at hepatic flexure and ascending colon. All pathological reports were consistent with chronic colitis without malignancy or organisms. Antineoplastic associated *C. difficile* diarrhea was diagnosed in 2 patients who had never received antibiotics within 2 months. Seventeen patients out of 21 patients with hematologic malignancy received antineoplastics before having CDAD. Metronidazole was prescribed as primary treatment in 82.3% with a response rate of 74.5%. Ten patients who did not respond to metronidazole treatment received oral vancomycin. Four of them received oral vancomycin 250 mg q 6 h and all of them had favorable response. The other 6 patients received oral

Table 1. Demographics, diagnosis, treatments and outcomes of 62 patients with CDAD

Characteristic	Finding
Gender: Females: Males	32: 30
Age, years: Mean (SD)	66.56 (16.63)
Symptoms and signs	
Diarrhea	62/62 (100%)
Abdominal pain/tenderness	6/27 (22.2%)
Fever	23/62 (37.1%)
Laboratory profiles	
Leukocytosis (WBC > 15,000 /uL)	15/62 (24.2%)
Leukopenia (WBC < 1,000 /uL)	7/62 (11.3%)
Hypoalbuminemia (serum albumin < 2.5 g/dl)	23/62 (37.1%)
Colonoscopy/Sigmoidoscopy	7/62 (11.3%)
Diagnosis of CDAD	
Positive CDT	53/62 (85.6%)
PMC by colonoscopy with negative CDT	3/62 (4.8%)
PMC by sigmoidoscopy with negative CDT	3/62 (4.8%)
Typical finding of PMC by abdominal CT with negative CDT and no typical endoscopic finding	1/62 (1.6%)
Typical finding of PMC by abdominal CT with negative CDT and no endoscopy performed	2/62 (3.2%)
Antibiotic use	60/62 (96.8%)
Type of Antibiotics	
Penicillin	4 (6.5%)
Cephalosporin (cefazolin, ceftriaxone, ceftazidime, cefepime)	39 (62.9%)
Beta lactam- Beta lactamase inhibitors (piperacillin-tazobactam, cefoperazone-sulbactam, ampicillin-salbactam, amoxicillin-clavulanate)	21 (33.9%)
Carbapenem (imipenem, meropenem, ertapenem)	29 (46.8%)
Fluoroquinolone (ciprofloxacin, levofloxacin)	15 (24.2%)
Amikacin	14 (22.6%)
Clindamycin	10 (16.1%)
Macrolide (roxithromycin, clarithromycin)	3 (4.8%)
Vancomycin	8 (12.9%)
Colistin	4 (6.5%)
Netilmicin	1 (1.6%)
Trimethoprim-sulfamethoxazole	2 (3.2%)
Chemotherapy	18/31 (58.1%)
Type of Chemotherapy	
Idarubicin plus cytarabine	4/18 (22.2%)
Idarubicin plus ATRA	1/18 (5.5%)
Hyper CVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone) plus L-asparaginase	1/18 (5.5%)
CHOP (cyclophosphamide, doxorubicin, vincristine and dexamethasone)	2/18 (11.1%)
COP (cyclophosphamide, vincristine and dexamethasone)	1/18 (5.5%)
ICE (ifosfamide, etoposide and carboplatin)	1/18 (5.5%)
CODOX-M (cyclophosphamide, vincristine, doxorubicin, cytarabine and methotrexate)	1/18 (5.5%)
Vinblastine, Cyclophosphamide plus Dexamethasone	1/18 (5.5%)
Vinblastin, Cytarabine, 6-TG(thioguanine) plus Dexamethasone	1/18 (5.5%)
Dexamethasone	1/18 (5.5%)
Bortezomib	1/18 (5.5%)
Thalidomide, Bortezomib and Prednisolone	1/18 (5.5%)
VAD (Doxorubicin, Vincristine, Dexamethasone)	1/18 (5.5%)
5 Fluorouracil plus leucovorin	1/18 (5.5%)
Treatment	
Discontinue current antibiotic (s)	3/62 (4.8%)

Table 1. Cont.

Characteristic	Finding
Response	3/3 (100%)
Metronidazole IV/PO for 10 d.	51/62 (82.3%)
Response	38/51 (74.5%)
No response	10/51 (19.6%)
Unknown*	3/51 (5.9%)
Vancomycin 250 mg PO q 6 h for 14 d.	1/62 (1.6%)
Response	1/1 (100%)
Metronidazole IV/PO and Vancomycin 250 mg PO q 6 h for 14 d.	1/62 (1.6%)
Response	1/1 (100%)
Spontaneous recovery without any treatment for CDAD	6/62 (9.7%)
Surgery	0
Mortality	
Death associated with CDAD	2/62 (3.2%)
Death from disease other than CDAD	21/62 (33.9%)
Recurrence of CDAD	2/62 (3.2%)

* All died after starting metronidazole treatment for only 2 days

vancomycin 125 mg q 6 h with the following responses: 2 patients responded, 1 patient died from a disease not associated with CDAD after 3 days of vancomycin, and 3 patients did not respond and the treatment was changed to oral vancomycin 250 mg q 6 h in which 2 of them died from CDAD, and 1 patient was transferred to his hometown hospital. Two patients had recurrent CDAD. The overall mortality was 37% in which 3.2% were related to CDAD.

Comparison of the characteristics of 62 patients with CDAD and 124 patients without CDAD are shown in Table 2. The characteristics significantly associated with a presence of CDAD were hematologic malignancy, receiving chemotherapy, proton pump inhibitor or immunosuppressive agent and nasogastric intubation.

The prevalence and patterns of antibiotic usage are shown in Table 3. Almost all patients in both groups received antibiotic (s) before developing diarrhea. Beta-lactams, especially cephalosporins, were the most common antibiotics given to the patients.

The univariate and multivariate analyses of the factors associated with CDAD are shown in Table 4. Univariate analysis showed that antibiotic use ($\geq$ 2 agents), PPI use, hematologic malignancy, and receiving chemotherapy or immunosuppressive agents were associated with CDAD. Multivariate logistic regression analysis revealed that only antibiotic use ($\geq$ 2 agents), PPI use and hematologic malignancy were independent risk factors associated with CDAD. Nasogastric intubation was observed to be associated with CDAD as a protective factor from both univariate and multivariate analyses.

Discussion

Prevalence of CDAD in suspected *C. difficile*-associated hospital-acquired diarrhea in hospitalized patients at Siriraj Hospital was 12.3% (95% CI 8.5% to 17.6%) which was lower than previous study in Thai adult patients reported in 2003[10]. This discrepancy could be due to a difference in diagnostic testing methods of *C. difficile* toxins. Polymerase chain reaction (PCR) technique was used in previous study[10]. Although PCR may be more sensitive and more specific, it needs more data on utility PCR. Cell cytotoxic assay is gold standard method for detecting CDT and recent reports indicated that 2-step algorithm, detecting glutamate dehydrogenase as initial screening and then using toxigenic culture as the confirmation test, has reasonably good sensitivity, specificity and cost-effectiveness[13]. However, the major disadvantages of such technique are that it is technically demanding and has a relatively long turnaround time (24-48h)[13,14]. Therefore, such a method is not routinely used in most hospital laboratories including Siriraj Hospital. Multiple EIA test may increase the diagnostic yield by 5%-10%[15] but it also increases the cost. Since we did not repeat the test in most cases, we might miss some cases of CDAD. Another explanation would be related to specimen collection and transportation. McFarland[16]

Table 2. Comparison of the characteristics of the patients with CDAD (62 cases) and without CDAD (124 cases)

Characteristic	CDAD (n = 62)	No CDAD (n = 124)	OR (95% CI)	p
Gender				
Females: Males	32: 30	64: 60		1
Age (years)				
Mean (SD)	66.56 (16.63)	66.69 (16.62)		1
Range	(26-95)	(25-95)		
Co-morbidity				
Diabetes Mellitus	21 (33.9%)	44 (35.5%)	0.93 (0.49-1.77)	0.83
Neurologic disease	16 (25.8%)	37 (29.8%)	0.82 (0.41-1.63)	0.57
Hematologic malignancy	21 (33.9%)	18 (14.5%)	3.02 (1.46-6.23)	0.002
Acute leukemia	9 (14.5%)	8 (6.5%)	2.46 (0.90-6.74)	0.072
Lymphoma	9 (14.5%)	8 (6.5%)	2.46 (0.90-6.74)	0.072
Chronic leukemia	1 (1.6%)	0	-	0.33
Multiple myeloma	2 (3.2%)	2 (1.6%)	2.03 (0.28-14.79)	0.41
Malignant solid tumor	10 (16.1%)	27 (21.8%)	0.69 (0.31-1.54)	0.36
Chemotherapy for malignancy	18 (29%)	20 (16.1%)	2.13 (1.03-4.41)	0.04
Respiratory tract disease	7 (11.3%)	11 (8.9%)	1.31 (0.48-3.56)	0.59
Connective tissue diseases	2 (3.2%)	2 (1.6%)	2.03 (0.28-14.79)	0.41
HIV-infection	1 (1.6%)	2 (1.6%)	1 (0.09-11.25)	1
Surgery	13 (21%)	26 (21%)	1 (0.47-2.12)	1
Pregnancy	1 (1.6%)	0	-	0.33
Solid organ transplantation	0	1 (1.6%)	-	1
Others				
Renal disease	10 (16.1%)	23 (18.5%)	0.84 (0.37-1.91)	0.68
Cardiac disease	11 (17.7%)	38 (30.6%)	0.49 (0.23-1.04)	0.06
Hepatic disease	3 (4.8%)	9 (7.3%)	0.65 (0.17-2.49)	0.75
Hypertension	23 (37.1%)	65 (52.4%)	0.54 (0.29-1.00)	0.05
Dyslipidemia	9 (14.5%)	27 (21.8%)	0.61 (0.27-1.39)	0.24
Other diseases	13 (21%)	17 (13.7%)	1.67 (0.75-3.71)	0.21
Medications				
Immunosuppressive agent	20 (32.3%)	23(18.5%)	2.09 (1.04-4.21)	0.037
Proton pump inhibitor	55 (88.7%)	93 (75%)	2.62 (1.08-6.35)	0.029
H2 blocker	0	1 (0.8%)	-	1
Nasogastric intubation	17 (27.4%)	64 (51.6%)	0.35 (0.18-0.69)	0.002
Laboratory findings				
Leukopenia (WBC < 1,000 /uL)	7 (11.3%)	8 (6.5%)	1.85 (0.64-5.25)	0.25
Serum albumin <2.5 mg/dl	23 (37.1%)	36 (29.0%)	1.44 (0.76-2.75)	0.27
Multiple CDT test (≥2)	25 (40.3%)	25 (20.2%)	2.68 (1.37-5.23)	0.003

found that false negative results occurred in 29% to 56% of cases, while this study showed only 14.5% (9/62 cases). False negative results may occur when the specimens are not promptly tested or not immediately stored in refrigerator because *C. difficile* toxin degrades at room temperature and may be undetectable within 2 h after collection of stool specimen. Stool specimens from the patients in our study were usually kept at room temperature until transport to the microbiology laboratory. Information on time intervals from collecting stool specimens and transporting the specimens to laboratory were not available.

Regarding the risk factors of CDAD, being an elderly patient (> 65 years) is one of the main risk for CDI[6,8,17,18]. The mean age of 62 patients with CDAD in our study was 66 years. However, our case control study was designed to match cases with controls in terms of gender and age. Therefore, we were unable to document if older age was a risk factor of CDAD. Previous studies revealed that major risk factors for

Table 3. The prevalence and pattern of antibiotic usage

	CDAD (n = 62)	No CDAD (n = 124)	OR (95%CI)	p
Number of recent antibiotic use ≥ 2 agents*	60 (96.8%)	64 (51.6%)	5.43 (1.26-8.03)	0.014
Type of antibiotic				
Penicillin	4 (6.5%)	10 (8.1%)	0.78 (0.24-2.62)	0.77
Cephalosporin	39 (62.9%)	75 (60.5%)	1.11 (0.59-2.08)	0.75
BLBI	21 (33.9%)	54 (43.5%)	0.66 (0.35-1.25)	0.21
Carbapenem	29 (46.8%)	54 (43.5%)	1.14 (0.62-2.10)	0.68
Fluoroquinolone	15 (24.2%)	23 (18.5%)	1.40 (0.67-2.93)	0.37
Amikacin	14 (22.6%)	22 (17.7%)	1.35 (0.64-2.81)	0.44
Clindamycin	10 (16.1%)	20 (16.1%)	1.0 (0.44-2.29)	1
Macrolide	3 (4.8%)	6 (4.8%)	1.0 (0.24-4.14)	1
Vancomycin	8 (12.9%)	32 (25.8%)	0.43 (0.18-0.99)	0.04
Colistin	4 (6.5%)	9 (7.3%)	0.88 (0.26-2.98)	1
Fosfomycin	0	3 (2.4%)	-	0.55
Tigecycline	0	1 (0.9%)	-	1
Co-trimoxazole	2 (3.2%)	6 (4.8%)	0.66 (0.13-3.35)	0.72
Metronidazole	0	2 (1.6%)	-	0.55
Doxycycline	0	1 (0.8%)	-	1

Table 4. Univariate and multivariate analyses of the factors associated with CDAD

Factor	Univariate Analysis		Multivariate Analysis	
	OR (95%CI)	P	OR (95%CI)	P
Number of recent antibiotic use ≥ 2 agents	5.43 (1.22-24.12)	0.014	6.58 (1.39-30.91)	0.017
Proton pump inhibitor	2.62 (1.08-6.35)	0.029	3.27 (1.27-8.4)	0.014
Hematologic malignancy	3.02 (1.46-6.23)	0.002	2.41 (1.08-5.38)	0.032
Chemotherapy for malignancy	2.13 (1.03-4.41)	0.04	-	
Immunosuppressive agents	2.09 (1.04-4.21)	0.037	-	
Nasogastric intubation	0.35 (0.18-0.69)	0.002	0.36 (0.17-0.74)	0.005

CDAD were antibiotic exposure, particularly clindamycin, cephalosporins and other beta-lactams[1,10,19]. Fluoroquinolones have recently been implicated as a risk factor of CDI[6,20,21]. Use of combination antibiotic therapy and long-term receipt of antibiotic therapy are also risk factors. The risk of CDI was also increased among patients who received short-term preoperative antibiotic prophylaxis[5], after emergency operations and among patients who have undergone intestinal resection[22] or total joint arthroplasty[23]. Other factors were usage of proton pump inhibitor (PPI) medications[24], underlying disease severity[10], multiple co-morbidities[25], prolonged stay in health-care settings[26], post solid organ transplantation[27-29], peripartum[30], hypoalbuminemia[26], antineoplastic medication[31,32], acute leukemia[33] and nasogastric intubation intubation[34,35]. Our study revealed that exposure to multiple antibiotics (≥ 2 agents) was significant risk factor for CDAD. Some antibiotics such as cephalosporin, carbapenem, fluoroquinolone and aminoglycoside were prescribed more commonly in patients with CDAD without statistically significant difference from those without CDAD. Patients who underwent surgical procedure and received preoperative antibiotic prophylaxis were not significantly different in both groups. We found that PPI, hematologic malignancy, receiving chemotherapy or immunosuppressive agent were risk factors for

developing CDAD in univariate analysis. However, only multiple antibiotics (≥ 2 agents), PPI and hematologic malignancy were independent risk factors associated with CDAD from multivariate logistic regression analysis. Proton pump inhibitor was found to be a significant risk factor from a systematic review of 12 papers evaluating 2,948 patients[36] and the study reported by Dial et al[25]. Gastric acid is postulated to be an immune defense against gastrointestinal infection including CDAD[37-39] and PPI may compromise such defense. Therefore, PPI should be used cautiously in hospitalized patients.

C. difficile infection is not rare and should be suspected whenever a hospitalized patient with neutropenia develops diarrhea[40]. Seven patients with neutropenia in our series developed CDAD.

Non-antibiotic associated *C. difficile* colitis has been reported, especially in those who received antineoplastic agents. Prevalence of antineoplastic-associated *C. difficile* colitis in previous report from Thailand was 20%[32]. Our study found only 2 cases of antineoplastic-associated colitis (7.4%). Chemotherapy-associated infection with *C. difficile* may be underreported because it is not suspected or because most of the patients also received concomitant antibiotics. Only one patient with CDAD in our study was a pregnant woman who also had multiple risks for CDI such as antibiotic exposure, cesarean section and chemotherapy for acute leukemia. Clinicians should consider *C. difficile* infection in pregnant and peri-partum patient with diarrhea even if she does not have traditional risk factors for *C. difficile* infection[30]. Interestingly, our study observed that nasogastric intubation was significantly associated with CDAD as a protective factor. This observation is in contrast with previous reports demonstrating that nasogastric intubation was a risk factor for CDAD[34,35]. Nasogastric intubation may decrease a risk of CDAD by preventing the patients from receiving foods contaminated with *C. difficile*. This hypothesis needs further study.

Metronidazole has been recommended as initial therapy for CDI since the late 1990s and continues to be the first choice for therapy of CDI. However, oral vancomycin is recommended in seriously ill patients and those with complicated or fulminant infections or multiple recurrences of CDI. Metronidazole was used as an initial antibiotic in most of the patients (82.3%) in our study with a mean duration of 10 days. A non-response rate of metronidazole of 19.6% in our study was comparable to other studies reported by Pepin[41] (25.7%), Musher DM[42] (22%) and Wafa (29%)[43,44]. A formulation of vancomycin to be given orally is not available in Thailand and parenteral formulation of vancomycin is given orally to CDI patients who need oral vancomycin. Oral vancomycin was given to 12 patients in our study due to severe CDAD (2 patients) and poor response to metronidazole (10 patients). Three out of 10 patients (33%) who received oral vancomycin did not respond to therapy and 2 of them died from CDAD. A comparison of efficacy of oral vancomycin between parenteral forrmulation with oral formulation for therapy of CDI has never been reported. A study on therapy of CDI using parenteral formulation of vancomycin given orally should be done in order to determine if such therapy is efficacious in situations when oral formulation of vancomycin is not available. Two patients in our study had recurrent CDAD. One was an elderly man who had been hospitalized for 6 months during which he received a prolonged course of antibiotics and PPI. Another patient had SLE who received PPI. It was found that patients receiving PPI were more likely to have recurrent CDI[36]. The factors associated with increasing the risk of recurrent CDI are inadequate immune response to *C. difficile* toxins and persistent disruption of normal colonic florae. Current guidelines recommend that the first recurrent episode be treated with the same agent (metronidazole or vancomycin) used for the previous episode. If the first recurrence is severe, oral vancomycin should be used. Important epidemiologic risk factors include advanced age, continuation of other antibiotics, and prolonged hospital stay[45].

The mortality rate from CDAD in our study (3.2%) was comparable to other reports by Schroeder[46] (1%-2.5%) and Zilberberg[47] (2.3%). There were reports on a hypervirulent strain of *C. difficile* called NAP1/BI/027 that was associated with increased morbidity and mortality in North America and Europe[48,49]. Typing of *C. difficile* strains isolated from fatal cases in our study was not performed.

Potential conflicts of interest

None.

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ระบาดวิทยาโรคอุจจาระร่วงในโรงพยาบาลจาก *Clostridium difficile* ที่โรงพยาบาลศิริราช

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ภูมิหลัง: *สาเหตุสำคัญของโรคอุจจาระร่วงในโรงพยาบาลคือการติดเชื้อ Clostridium difficile*

วัตถุประสงค์: *เพื่อทราบความชุก ปัจจัยเสี่ยง การวินิจฉัย การรักษาและผลการรักษาโรคอุจจาระร่วงในโรงพยาบาลที่เกิดจาก C. difficile ในผู้ป่วยที่รับไว้รักษาที่โรงพยาบาลศิริราช*

วัสดุและวิธีการ: *ทบทวนเวชระเบียนผู้ป่วยอายุตั้งแต่ 14 ปี ที่รับไว้รักษาในรงพยาบาลศิริราชที่เกิดโรค อุจจาระร่วงในโรงพยาบาลซึ่งสงสัยการติดเชื้อ C. difficile และส่งตรวจ C. difficile toxin ตั้งแต่มีนาคมถึงมิถุนายน พ.ศ. 2551 การศึกษาปัจจัยเสี่ยงต่อการเกิดโรคอุจจาระร่วงจาก C. difficile ทำโดยเปรียบเทียบข้อมูลกลุ่มผู้ป่วยที่เป็นโรคอุจจาระร่วงในโรงพยาบาลจาก C. difficile กับผู้ป่วยที่เป็นโรคอุจจาระร่วงในโรงพยาบาลจากสาเหตุอื่น โดยผู้ป่วยทั้งสองกลุ่มมีอายุและเพศที่คล้ายคลึงกัน*

ผลการศึกษา *: ความชุกของโรคอุจจาระร่วงในโรงพยาบาลจากการติดเชื้อ C. difficile ร้อยละ 12.3 (ความเชื่อมั่นร้อยละ 95 อยู่ระหว่างร้อยละ 8.5 ถึงร้อยละ 17.6) ปัจจัยเสี่ยงต่อการเกิดโรคอุจจาระร่วงจาก C. difficile ด้วยการวิเคราะห์ univariate คือ การได้รับยาต้านจุลชีพตั้งแต่สองขนานขึ้นไป, มะเร็งของเม็ดเลือด, การได้รับ proton pump inhibitor, การได้รับยาเคมีบำบัดหรือยากดภูมิคุ้มกัน แต่การวิเคราะห์ multivariate พบว่าปัจจัยเสี่ยงต่อการเกิดโรคอุจจาระร่วงจาก C. difficile คือ การได้รับยาต้านจุลชีพตั้งแต่สองขนานขึ้นไป, มะเร็งของเม็ดเลือด, การได้รับ proton pump inhibitor ส่วนการใส่สายให้อาหารทางจมูกมีความสัมพันธ์ในการลดการเกิดโรค การวินิจฉัยโรคอุจจาระร่วงในโรงพยาบาลจากการติดเชื้อ C. difficile มักอาศัยการตรวจพบ C. difficile toxin ในอุจจาระ ผู้ป่วยตอบสนองต่อการรักษาด้วย metronidazole ร้อยละ 74.5 อัตราการกลับเป็นโรคซ้ำร้อยละ 3.2 และอัตราตายจากโรคอุจจาระร่วงในโรงพยาบาลจากการติดเชื้อ C. difficile ร้อยละ 3.2.*

สรุป: *โรคอุจจาระร่วงที่เกิดในโรงพยาบาลจากการติดเชื้อ C. difficile พบได้บ้างโดยเฉพาะผู้ป่วยที่ได้รับยาต้านจุลชีพตั้งแต่สองขนานขึ้นไป, มะเร็งของเม็ดเลือด, ได้รับ proton pump inhibitor ยา metronidazole ยังรักษาโรคนี้ได้ผลดีในผู้ป่วยส่วนมาก อัตราการกลับเป็นโรคซ้ำและอัตราตายจากโรคนี้มีน้อย*