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3차 의료기관에서 *Clostridium difficile*-associated Diarrhea의 발생빈도 및 치료에 관한 연구

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Frequency of *Clostridium difficile*-associated Diarrhea and Relevant Medical Treatment in a Tertiary Care Hospital in Korea

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배경: 약물로 인한 *Clostridium difficile*-associated diarrhea (CDAD)는 널리 알려져 있으며 우리나라에서 항생제와 프로톤 펌프 억제제 소모량을 고려할 때 질환 치료과정에서의 CDAD 발생빈도 및 CDAD 유발 이전에 투여한 약물의 사용빈도와 CDAD의 치료방법을 조사할 필요성이 있다.
방법: 경상대학교 병원에서2011년 1월부터 6월까지의 입원환자를 대상으로 대변 독소 검사에 의해 CDAD로 판명된 환자의 성별, 연령분포, 질환명, 입원병동, 재발률을 조사하였으며 CDAD 판명이전에 투여한 약제 및 CDAD 판명 후 치료약제를 조사하였다.
결과: 연구기간 동안 CDAD 대변 독소 검사 의뢰된 환자수는 1,500명이었으며 CDAD 양성은 111명(9.3%)이었고, 재발은 29명(26.1%)이었다. CDAD를 주소로 입원한 환자는 17명 (15.3%)이었고, 나머지는 입원기간 중에 발생하였다. CDAD 양성인 환자의 연령대는 60대에서 32.4% (36/111명) 이었고, 내과병동에서 34.2%를 나타내었고, 재발률은 외과계 병동에서 41.4%로 가장 높게 나타났다. CDAD 환자의 17% (19/111명)은 항암제 투여 동안 발생하였으며 CDAD 발생 전 사용약물로는 세팔로스포린계 항생제가 162회로 가장 빈번하게 사용 되었으며, 히스타민2 수용체 길항제 107회, 스테로이드 82회, 비 스테로이드 항염제 79회, 프로톤 펌프 억제제 77회, 하제 59회, 항암제가 33회 처방되었다. CDAD 치료약제로는 8종의 약제가 241회 처방 되었으며 metronidazole이 99회로 가장 빈번하게 사용되었고, vancomycin이 37회로 나타났다.
결론: 입원환자에 있어서 CDAD양성은 특히 고령의 암환자가 많아 항암제 투여 시에는 CDAD 발생에 주의해야 할 것으로 보인다. CDAD의 치료약제로는 metronidazole이 vancomycin 보다 많이 사용되는 것으로 나타났다.

□ Key words - *Clostridium difficile*-associated diarrhea (CDAD), colitis, nosocomial

INTRODUCTION

The most common cause of hospital-acquired diarrhea is *Clostridium difficile*-associated diarrhea (CDAD).[1, 2] *C. difficile* can cause pseudomembranous colitis (PMC) and severe colon infection induced by the eradication of normal gut flora after a long exposure to broad spectrum antibiotics. *C. difficile* causes most cases of PMC while it does 15-25% of antibiotic-associated diarrhea. The severity of illnesses due to this organism varies from asymptomatic infections to serious complications such as megacolon or colon perforation. Even though diseases caused by *C. difficile* have been recognized generally mild and non-fatal, disease incidence and severity have increased recently.[3-5]

Clostridium difficile is an anaerobic, spore-forming, and Gram-positive rod producing exotoxins that are pathogenic to humans. Sporulation enhances bacterial

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survival in the environment, especially in hospital settings. Cross infection in the same ward or in the same room of a hospital may result in a nosocomial outbreak. *C. difficile* is known to infect individuals receiving antibiotic therapy, severely ill patients who are hospitalized, and residents of long-term care facilities.[6)]

C. difficile is a normal component of the commensal gut flora, and it is especially common in neonates, with a prevalence rate of approximately 50% in this population. In medical procedures, the known risk factors associated with the development of CDAD include gastrointestinal (GI) surgery, the use of a feeding tube, environmental exposure, advanced age, and the severity of comorbid conditions. In regards to medication usage, prior exposure to antibiotics, antineoplastic agents, nonsteroidal antiinflammatory drugs (NSAIDS), H2 antagonists, antimotility agents, and steroids are well known risk factors for CDAD. Recently, proton pump inhibitors used to treat gastric ulcers have been identified as novel agents that cause CDAD.[7-9)] These factors may disrupt the stability of normal gut flora and enhance *C. difficile* colonization.

In addition, *C. difficile* can cause infection in healthy individuals in the community. Recently an increased incidence of community-acquired CDAD (CA-CDAD) has been observed even though CDAD has been traditionally considered as a hospital-acquired infection. Although community-acquired infections are currently less common, it is possible that they can spread widely and induce higher rates of complications due to exposure in various environments.[10)]

Because of the high use of antibiotics and proton pump inhibitors in Korea, CDAD is a major concern. This study documented the high incidence of CDAD in Gyeongsang National University Hospital, which is located in southeast Korea, and assessed the frequency of CDAD and relevant treatment.

METHODS

Study population

A retrospective case study design was used. This study included 140 cases that showed a positive reaction in the stool toxin assay for *C. difficile* among 1,500 cases requested for laboratory confirmation between January and June of 2011 at Gyeongsang National University Hospital (GNUH). GNUH is a 910-bed tertiary care hospital that is comprised of 30 units including but not limited to internal medicine, surgery, hematology, emergency, and intensive care. The number of patients included in this study was 111 since 29 cases were recurrent among 140 cases. The 140 CDAD positive cases were collected without considering of age and gender. The demographic data including age, gender, admitted ward, hospitalization period, and underlying illnesses were also recorded. A total of 12,617 patients were admitted to GNUH during this study period.

Detection of *C. difficile* toxin

When patients presented with diarrhea, stool specimens were evaluated for the presence of *C. difficile* toxin. The toxin assays were performed using the VIDAS enzyme immunoassay system (bioMerieux, Durham, NC, USA) that detects *C. difficile* toxins A and B (CDAB). After centrifugation of stool specimens combined with a mixing reagent, the supernatants (300 μL) were applied to CDAB enzyme immune assay (EIA) kits. Relative fluorescence values (RFV) over 1.0 were regarded as positive, whereas RFV between 0.4–1.0 were recorded as equivocal; RFV below 0.4 were recorded as negative. The patients who exhibited RFV over 1.0 were selected for the study.

Medications taken prior to CDAD

Lists of medications taken prior to CDAD and comorbidities were documented through electrical medical record (EMR) in GNUH. Patient exposure to predisposing medications prior to CDAD diagnosis was recorded based on the following drug categories: antibiotics, antifungal agents, antivirals, anti-neoplastic agents, NSAIDS, H2 antagonists, immunosuppressants, stool softeners or laxatives, steroids, and proton pump inhibitors. When multiple medications were prescribed, each medication was counted.

CDAD treatment

Treatment regimens against CDAD were documented using EMR. The number of medications in the treatment regimen against CDAD was noted for each patient. Treatment medications such as metronidazole, vancomycin, rifaximin, teicoplanin, adsorbents and antimotility agents were recorded.

Admitted wards and hospitalization period

Admitted hospital wards were documented. In addition, hospitalization periods prior to CDAD diagnosis were noted. The hospitalization period of patients admitted with CDAD was recorded as the period of zero.

RESULTS

CDAD subjects

Based on the *C. difficile* stool toxin assay, 140 cases were identified as CDAD positive among 1,500 cases with diarrhea that were requested for laboratory confirmation over a 6-month period, resulting in a CDAD positive rate of 9.3% (140/1,500). These 140 CDAD cases included 111 patients since 29 patients showed relapsing episodes. Of these patients, 84.7% (94/111) acquired CDAD during hospitalization, while 17 patients (15.3%) presented with CDAD prior to hospitalization (Figure 1). The incidences of CDAD amounted to 0.88% (111/12,617) of total hospital admissions during the study period.

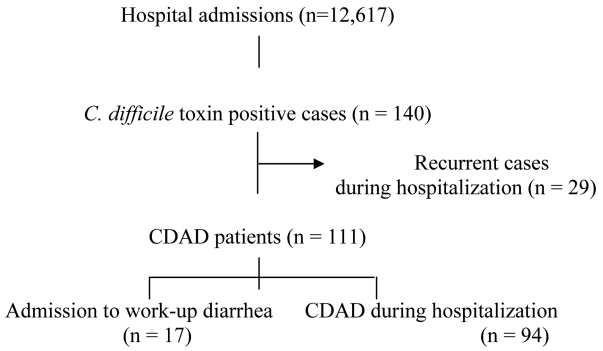

Fig. 1. Categorization of *Clostridium difficile*-associated diarrhea cases in Gyeongsang National University Hospital.

Table 1. Demographics of *Clostridium difficile*-associated diarrhea patients

Age range	Male	Female	Total
1~10 y	1	1	2
11~20 y	2 (1)	0	2 (1)
21~30 y	1	0	1
31~40 y	1 (3)	3	4 (3)
41~50 y	3 (2)	3 (1)	6 (3)
51~60 y	8 (1)	6	14 (1)
61~70 y	21 (2)	15 (6)	36 (8)
71~80 y	19 (7)	14	33 (7)
81~90 y	7 (3)	6 (3)	13 (6)
Total	62 (19)	49 (10)	111 (29)

( ): recurrence

CDAD patient demographics

Advanced age was associated with CDAD occurrence. The number of recurrent cases was also related to increased age (Table 1, Figure 2). The highest occurrence (32.4%, 36 out of 111 patients) was observed in patients aged between 61 and 70 years. The highest recurrence (27.6%, 8 out of 29) was observed in the same patient age range as well.

CDAD comorbidities

Coexisting health conditions included, in decreasing order of prevalence, cancer, infection, cerebral disorders, skeletomuscular disorders, renal disorders, respiratory disorders, gastrointestinal disorders, and cardiovascular disorders (Table 2). In terms of prevalence of comorbid conditions, 17% of 111 CDAD patients had cancer and 15.3% of CDAD patients also presented with an infection. Seventeen (15.3%) patients were admitted to the hospital due to diarrhea.

Medications taken prior to CDAD

In total, 102 different medications were prescribed prior to CDAD identified. They were prescribed a total of 849 times. Of these medications, cephalosporins were prescribed 162 times (19%). Antibiotics were prescribed a total of 371 times, followed by H2 antagonists (107 times), steroids (82 times), NSAIDs (79 times), PPIs (77 times), laxatives (59

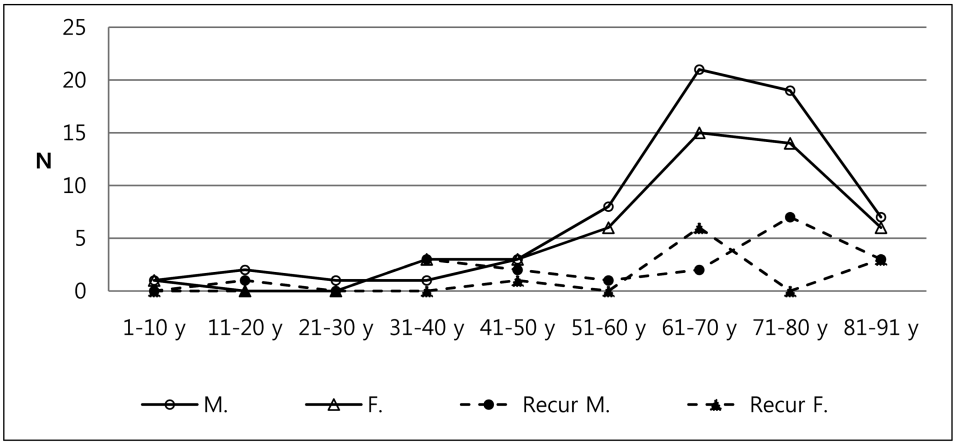

Fig. 2. Age distribution of *Clostridium difficile*-associated diarrhea.

Table 2. Comorbidities in 111 patients with *Clostridium difficile*-associated diarrhea

Comorbid conditions	N (%)
Cancer	19 (17.0)
Diarrhea	17 (15.3)
Infection	17 (15.3)
Cerebral disorders	16 (14.4)
Skeletomuscular disorders	10 (9.0)
Renal disorders	7 (6.3)
Respiratory disorders	5 (4.5)
Gastrointestinal disorders	4 (3.7)
Cardiovascular disorders	4 (3.7)
Others	5 (4.5)
Unknown	7 (6.3)
Total	111

times), and antineoplastics (33 times) (Table 3).

CDAD treatment regimens

Eight medications were prescribed to treat CDAD. Metronidazole was written for 99 times (41.1%) out of 241 prescriptions; oral vancomycin was the next most common drug selected, with 37 prescriptions. Absorbent, antispasmotics, and antimotility agents were used 45, 29, and 18 times, respectively (Table 4).

Admitted wards and hospitalization

CDAD occurred most commonly in the internal medicine ward (34.2%, 48/140 cases), followed by the surgery ward, the oncology ward, and the intensive care unit. Of the 29 recurrent cases, 41.4% were identified in the surgery ward (Table 5). However, no relationship between length of hospitalization and CDAD occurrence was observed. CDAD occurrence was 24.3% (27/111 patients) within 10 days of hospitalization and 18.0% (20/111 patients) within 20 days of hospitalization.

DISCUSSION

C. difficile is a normal inhabitant of the gut. Spore formation by these bacteria enhances their ability to survive in the environment for long periods of time. Spores are more resistant to disinfectants compared to other bacteria. Once *C. difficile* are secreted from an infected patient, they can contaminate the toilet, bathtub, faucet, floor, bed rail, bedspread, or clothes. Medical personnel, patient attendants, as well as other patients nearby can become infected and potentially harbor the bacteria as asymptomatic carriers. A vicious cycle of cross infection in hospital settings can cause *C. difficile* epidemics.[6)]

Although cytotoxin assay is the gold standard for diagnosis of *C. difficile* infection, it is less practical due to the requirement of complicated cell culture techniques. Previously, enterotoxin detection using an enzyme immunoassay (EIA) was widely used due to the convenience of the automated procedure.[11)] However, toxin A-, toxin B+ strains of *C. difficile* have recently been reported in our country, which was not

Table 3. Medications taken prior to *Clostridium difficile*-associated diarrhea

Antibiotics (371)
- Cephalosporins (162)
  - Ceftriaxone (30) Cefpodoxime (22)
  - Cephtriaxone (20) Cefotaxime (18)
  - Cefotiam (17) Cefazolin (16)
  - Cefepime (8) Cefoxitin (7)
  - Cefmenoxime (6) Cefuroxime (5)
  - Cefaclor (3) Cefotetan (3)
  - Ceftazidime (3) Cefditoren (1)
  - Cefixime (1) Cephadroxil (1)
  - Cefoperazone+Sulbactam (1)
- Penicillins (64)
  - Piperacillin+Tazobactam (40)
  - Sulbactam+Ampicillin (10)
  - Amoxicillin+Clavulanate (7)
  - Amoxicillin (2) Ampicillin (2)
  - Nafcillin (2) Piperacillin (1)
- Fluoroquinolones (60)
  - Ciprofloxacin (50) Levofloxacin (7)
  - Moxifloxacin (2) Gemifloxacin (1)
- Carbapenems (20)
  - Meropenem (14) Ertapenem (2)
  - Imipenem+Cilastatin (4)
- Clindamycin (19)
- Macrolides (18)
  - Azithromycin (16) Clarithromycin (2)
- Aminoglycosides (15)
  - Amikacin (7) Isepamicin (5)
  - Gentamicin (1) Netilmicin (1)
  - Tobramycin (1)
- Doxycycline (1)
- Miscellaneous (12)
  - Trimethoprim+Sulfamethoxazole (8)
  - Linezolid (2) Colistimethate (1)
  - Tigecycline (1)
- H2 antagonists (107)
  - Ranitidine (78) Cimetidine (10)
  - Famotidine (19)

Steroids (82)
- Dexamethasone (35) Prednisolone (22)
- Methylprednisolone (13)
- Hydrocortisone Sod. Succinate (12)

NSAIDs (79)
- Diclofenac sodium (30) Piroxicam (14)
- Zaltoprofen (8) Ketorolac (5)
- Ibuprofen +Codeine +Acetaminophen (6)
- Aceclofenac (2) Celecoxib (4)
- Morniflumate (5) Meloxicam (1)
- Naproxen (3) Protacin (1)

PPIs (77)
- Pantoprazole (45) Rabeprazole (23)
- Lansoprazole (9)

Laxatives (59)
- Bisacodyl (27) Lactulose (18)
- Lactitol(9) Alaxyl® granule (2)
- Calcium Polycarbophil (2)
- Agio® granule (1)

Antineoplastics (33)
- Cisplatin (3) Erlotinib (3) Etoposide (3)
- Gemcitabin (3) Anastrozole (2)
- Bicalutamide (2) Docetaxel (2)
- Ifosfamide (2) Vinorelbine (2)
- Bortezomib (1) Carboplatin (1)
- Cyclophosphamide (1) Cytarabine (1)
- Danazol (1) Doxorubicin (1)
- Irinotecan (1) L-Asparaginase (1)
- Methotrexate (1) Paclitaxel (1)
- Thymoglobulin (1)

Antifungals (29)
- Fluconazole (17) Itraconazole (6)
- Amphotericin B (4) Terbinafine (2)

Antivirals (9)
- Acyclovir (3) Oseltamivir (3)
- Famciclovir (2) Ganciclovir (1)

Immunosuppressants (3)
- Mycophenolate Mofetil (1)
- Cyclosporine (1)
- Tacrolimus (1)

( ): the number of prescriptions, total n = 849.

Table 4. Treatment regimens against *Clostridium difficile*-associated diarrhea

Classification	Medication	N (%)
Antibiotics	Metronidazole Tab	99 (41.1)
	Vancomycin Cap	37 (15.4)
	Rifaximin Tab	2 (0.8)
	Teicoplanin	2 (0.8)
Adsorbent	Dioctahedral smectite	45 (18.7)
Antispasmodic agent	Hyspan (Hyoscine-N-butylbromide)	29 (12.0)
Antimolility agent	Loperamide	18 (7.5)
Laxative	Polyethylene glycol 3350	9 (3.7)

Table 5. Admitted ward of patients with *Clostridium difficile*-associated diarrhea

Hospital wards	N (%)	Recurrence, N (%)	Total (%)
Internal medicine	39 (35.2)	9 (31.1)	48 (34.2)
Nephrology	7 (6.4)	4 (13.8)	11 (7.9)
Respirology	12 (10.8)	2 (6.9)	14 (10.0)
Gastroenterology	12 (10.8)	3 (10.4)	15 (10.7)
Rheumatology	5 (4.5)		5 (3.6)
Cardiology	2 (1.8)		2 (1.2)
Endocrinology	1 (0.9)		1 (0.6)
Surgery	30 (27.0)	12 (41.4)	42 (30.0)
Neurosurgery	15 (13.5)	6 (20.7)	21 (15.0)
Orthopedic surgery	9 (8.1)	4 (13.8)	13 (9.3)
Plastic surgery	3 (2.7)		3 (2.1)
Thoracic surgery	3 (2.7)	2 (6.9)	5 (3.6)
Oncology	15 (13.5)	3 (10.3)	18 (12.9)
Intensive care units	6 (5.4)	1 (3.4)	7 (5.0)
Emergency department	6 (5.4)		6 (4.3)
Others	15 (13.5)	4 (13.8)	19 (13.6)
Neurology	6 (5.4)		6 (4.3)
Obstetrics/gynecology	3 (2.7)		3 (2.1)
Rehabilitation	3 (2.7)	4 (13.8)	7 (5.0)
Pediatrics	2 (1.8)		2 (1.2)
Urology	1 (0.9)		1 (0.6)
Total	111	29	140

detected by an EIA designed to detect only toxin A. A new reagent that detects both toxin A and toxin B has been developed recently, and the laboratory in GNUH used this reagent.

Although this study utilized only the toxin assay to diagnose *C. difficile* infection, diagnoses can also be confirmed with either colonoscopy or bacterial culture methods. CDAD detection sensitivity is highest in the toxin assay, with up to 80% sensitivity. If other cases detected by colonoscopy or bacterial culture had been included, the number of patients may have increased by at least 20%. Although colonoscopy is essential to diagnose pseudomembranous colitis, it is rather invasive, expensive, and requires extensive bowel preparation. As *C. difficile* is an obligate anaerobe, anaerobic culture systems are required for their propagation. Because *C. difficile* is found in neonates and in carriers, its presence in the intestinal flora is not always indicative of an infection. Therefore, the toxin assay is simple, fast, sensitive, and more diagnostic compared to colonoscopy or anaerobic culture.

C. difficile is the most common cause of nosocomial diarrhea worldwide, and CDAD is more common in the developed countries. The incidence of CDAD varies from 1 to 10 cases in every 1,000 hospital admissions.[12, 13] The incidence of CDAD has increased recently. In Korea, a study showed that the incidence of CDAD was 21.73 cases per 10,000 admitted patients between the year of 2003 and 2005, and it significantly increased to 71.71 cases per 10,000 admitted patients between the year of 2006 and 2008.[14] The risk factors for CDAD included advanced age, severe underlying illnesses, medication usage, and admission to the intensive care unit. As the elderly population is growing in our country, there is an increased likelihood that CDAD prevalence may rise substantially in the overall population.[15,16] In addition, the medications used to treat underlying health conditions, such as antibiotics, antifungals, antivirals, chemotherapeutic agents, and proton pump inhibitors, are widely consumed in our country. Exposure to clindamy-

cin and cephalosporin are well known risk factors for CDAD. However, new quinolones may also predispose individuals to CDAD.[17] Aminoglycosides, carbapenem, bacitracin, and rifampin rarely induce CDAD. [18]

In this study, the incidence of CDAD was 0.88% (111/12,617) during this study period, resulting in 87.97 CDAD patients per 10.000 admitted to hospital. This finding shows this incidence rate for CDAD is higher than levels detected in previous studies conducted in Korea. CDAD occurrence was associated with advanced age; additionally, the recurrence rate of CDAD was related to advance age. In GNUH, the highest occurrence (32.4%, 36 out of 111) was observed in individuals aged between 61 and 70 years. This finding is similar to previous studies that showed individuals aged > 65 or > 75 years were at a greater risk for hospital-acquired CDAD.[19, 20] Coexisting diseases and the use of medications known to result in CDAD predisposition were related to CDAD occurrence. In this study, the coexisting diseases included cancer, infection, cerebral disorders, skeletomuscular disorders, gastrointestinal disorders, renal disorders, respiratory disorders, and cardiovascular disorders. In particular, cancer and infection made up 17% and 15.3% of comorbidities, respectively. Thus, these patients were inevitably exposed to medications such as antineoplastic agents and antibiotics that result in CDAD predisposition. In regards to the medications taken prior to CDAD, antibiotics, including cephalosporins, were prescribed 43.6% out of 849 total prescriptions. This finding regarding cephalosporin use as a common risk factor for CDAD is consistent with previous studies examining cephalosporin use in patients. [14, 18] H2 antagonists and PPIs were used 107 times and 77 times, respectively, and it is inconclusive whether exposure to H2 antagonists and PPIs was related to CDAD development because a previous study found that exposure to PPIs or H2 antagonists did not increase the risk of CDAD development.[21] However, it is possible to be considered as a causative factor.[14, 22] Antineoplatics and quinolones should also be screened as potential CDAD predisposing agents.[19, 21, 23] In this study, antineoplastics were prescribed 33 times. Although antineoplastics were prescribed less frequently than antibiotics, cancer patients showed the highest incidence of CDAD (17%). This implies that hospital admitted patients with antineoplastic therapy should be treated with heighted consideration for potentially increased risk of CDAD occurrence.

To treat CDAD, treatment with antibiotics or other causing agents should be stopped. However, this scenario is difficult to apply due to underlying illnesses. Some strains show resistant to metronidazole. It is known that the administration of antibiotics decreases the resistance to colonization of *C.difficile* and diminishes microbial competence.[24, 25] This study found that metronidazole, vancomycin, rifaximin, and teicoplanin were prescribed as antimicrobials to treat CDAD. Of these medications, metronidazole was written for 99 times out of 241 (41.1%) prescriptions; vancomycin was the next most commonly prescribed drug, with 37 prescriptions. These findings may reflect that vancomycin was carefully prescribed because of concerns regarding vancomycin-resistant enterococci (VRE). However, oral vancomycin is very effective pharmacokinetically in the gut. As enterococci are also part of the normal gut flora, they may become resistant if exposed vancomycin. Many cases of VRE have occurred due to oral vancomycin treatment in Korea. Currently, the VRE rate is 20–40%. In addition, antimotility agents, including loperamide, were prescribed; however, these agents are not recommended to treat CDAD because they impair response and increase the risk of toxic megacolon.[26, 27] As significant portions of antibiotics are prescribed at the primary care level, pharmacists should be more vigilant and be aware of CDAD to prevent patients from experiencing unwanted complications.

In this study, CDAD occurred most commonly in the internal medicine ward (34.2%, 48/140 cases), followed by the surgery and oncology wards. Additionally, our data supported that the use of H2 antagonists, PPIs, antibiotics, and antineoplastic agents were related to the occurrence of CDAD.[14,19,21,23] Of the 29 recurrent cases, 41.4% were identified in the surgery ward that

treated patients with more antibiotics, providing evidence that CDAD incidence is related to the number of antibiotics.[19,23] However, there was no relationship between the length of hospital stay and CDAD occurrence (24.32% in 10 days, 18.01% in 20 days). Since there was no consideration about severity of the diseases and discharge rates in this study, it would need further examination including survival rates.[18] In addition, there may be possibilities of CA-CDAD or pre-exposure of the risk factors including medications.[19, 28, 29] Of the patients, the profile of medication exposure was not detected and will require further investigation.

Due to the design of this study, several limitations must be mentioned. This study did not include CDAD cases diagnosed by colonoscopy or anaerobic bacterial culture. The frequency or duration of diarrhea was also not investigated. The toxin assay request date was selected as the date of diarrhea onset after exposure to possible risk factors. It is unclear whether CDAD cases occurred because of exposure to the ward environments or because of the predisposing medication. The potential risk factors for CDAD such as advanced age, severe underlying illnesses, medication usage, and exposure to admission wards were not evaluated independently. In addition, these potential factors were not compared to those of other hospitals. It is unclear whether GNUH has more aged patients, or GNUH uses more antibiotics and antineoplastic agents than others. When multiple medications were used, drug interactions among the medications were not considered; thus, the role of drug interactions in CDAD predisposition remains to be investigated. For patients with CA-CDAD, a profile of medication exposure was not described. Instead of selecting diarrhea group, the author used the toxin assay positive group. Elderly population of admitted patients and disease incidence in our region may falsely affect to the incidence according to age and disease. As there are small numbers of patient group, it is difficult to draw a conclusion in terms of incidence or recurrence rate. Validity of toxin assay should be considered.

In conclusion, both CDAD positive rate and recurrence were related to advanced patient age. The existence of comorbid conditions was associated to CDAD, as comorbidities were related to the use of predisposing medications and ward placement following hospitalization. Among known CDAD predisposing drugs, cephalosporins, H2 antagonists, steroids, NSAIDs, PPIs, and antineoplastics were commonly prescribed. A higher occurrence of CDAD was observed in the internal medicine ward, whereas recurrence was most common in the surgery ward. Advanced age patients under the treatment of antineoplastics need to be especially careful in considering the potential occurrence of CDAD. Metronidazole was more frequently used than vancomycin to treat CDAD.

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