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Major article

Risk factors associated with interfacility transfers among patients with *Clostridium difficile* infection

Reda A. Awali MD, MPH *, Deepthi Kandipalli MD, Amina Pervaiz MD, Sandhya Narukonda MD, Urooj Qazi MD, Naveen Trehan MD, Teena Chopra MD, MPH

Division of Infectious Diseases, Detroit Medical Center & Wayne State University, Detroit, MI

Key Words:
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Background: Preventing the transmission of *Clostridium difficile* infection (CDI) over the continuum of care presents an important challenge for infection control.

Methods: A prospective case-control study was conducted on patients admitted with CDI to a tertiary care hospital in Detroit between August 2012 and September 2013. Patients were then followed for 1 year by telephone interviews and the hospital administrative database. Cases, patients with interfacility transfers (IFTs), were patients admitted to our facility from another health care facility and discharged to long-term care (LTC) facilities. Controls were patients admitted from and discharged to home.

Results: There were 143 patients included in the study. Thirty-six (30%) cases were compared with 84 (70%) controls. Independent risk factors of CDI patients with IFTs (compared with CDI patients without IFTs) included Charlson Comorbidity Index score ≥6 (odds ratio [OR], 5.30; $P = .016$) and hospital-acquired CDI (OR, 4.92; $P = .023$). Patients with IFTs were more likely to be readmitted within 90 days of discharge than patients without IFTs (OR, 2.24; $P = .046$). One-year mortality rate was significantly higher among patients with IFTs than among patients without IFTs (OR, 4.33; $P = .01$).

Conclusions: With the growing number of alternate health care centers, it is highly critical to establish better collaboration between acute care and LTC facilities to tackle the increasing burden of CDI across the health care system.

A recent report supported by the Centers for Disease Control and Prevention showed that the number of patients diagnosed with *Clostridium difficile* infection (CDI) in the United States approached a half million in 2011.[1] The increase in CDI was pronounced among older adults (≥65 years) and was associated with approximately 29,000 deaths.[1] CDI now is considered the most common cause of antimicrobial-associated and hospital-acquired diarrhea in the United States.[2,3] More importantly, it is more commonly identified as a serious health care–associated infection than methicillin-resistant *Staphylococcus aureus*.[3]

Acquisition of CDI in acute care hospitals (AHs) and long-term care facilities (LTCFs) can be attributed to 3 important sources: patients with CDI or recent resolution of CDI diarrhea, patients colonized with the microorganism, and environments contaminated with *C difficile* spores.[4] The most important risk factor for acquiring the *C difficile* pathogen is exposure to antibiotics and health care setting, including AHs and LTCFs.[5] Other important risk factors for CDI include advanced age and underlying comorbidities.[6] The incidence of CDI in older adults was found to be 5-10 times higher than that in younger adults.[3] Moreover, older adults were at significantly higher risk for severe and complicated disease.[7]

Over the last decade, the changes in hospital reimbursement and the aging baby boomers and increased life expectancy have caused a significant shift in health care delivery from AHs to LTCFs.[8,9] A report by the 2004 National Nursing Home Survey showed that 36% of U.S. nursing home residents were admitted directly from AHs,[10] therefore making the interfacility patient sharing one of the important avenues for CDI transmission.[11] The Society for Healthcare Epidemiology of America reported that the number of CDI patients discharged directly from AHs to LTCFs doubled between 2000 and 2003.[12] Although CDI is increasingly being encountered in LTCFs,

* Address correspondence to Reda A. Awali, MD, MPH, Division of Infectious Diseases, Harper University Hospital, 5 Hudson, 3990 John Rd, Detroit, MI 48201.
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preventing CDI transmission over the continuum of care between AHs and LTCFs still embodies an important challenge for infection control and prevention.[13] Therefore, we conducted this study to better understand the epidemiology of CDI and the role of interfacility sharing practices in spreading CDI across the continuum of care. The aim of the current study was to investigate risk factors associated with interfacility transfers (IFTs) among CDI patients and compare the clinical outcomes of CDI patients with and without IFTs.

METHODS

Design and setting

This was an institutional review board–approved prospective case-control study conducted at a tertiary care hospital in metropolitan Detroit. Patients participating in the study were admitted to our hospital with a diagnosis of CDI (ICD-9 code 008.45) between August 2012 and September 2013. Patients were followed-up monthly via phone calls for 1 year after their index CDI diagnosis.

Definitions and inclusion criteria

Patients were initially identified through the electronic microbiologic database. Electronic medical records (EMRs) were then screened for clinical symptoms of CDI, particularly diarrhea with ≥3 unformed bowel movements within 24 hours of stool sampling.[12] Cases or patients with IFTs were defined as patients admitted directly to our facility from another health care facility (including AHs and LTCFs) and discharged thereafter to LTCFs. LTCFs described herein included long-term AHs, skilled nursing homes, rehabilitation centers, assisted-living facilities, and other chronic nursing homes.[14] Controls were patients presenting to our hospital from home and discharged thereafter to home. Patients with positive history of CDI within 3 months of the index CDI date were not included in the study.

Measures

All data pertaining to potential risk factors were collected 60 days prior to index admission using the hospital EMRs. Data collected for each participant included the following: (1) demographics (age, sex, and race), presenting symptoms, and comorbidities; (2) prior gastrointestinal endoscopic or surgical procedures and prior use of medications, including antibiotics, proton pump inhibitors, diuretics, laxatives, opioids, and immunosuppressants; and (3) laboratory biomarkers, such as serum creatinine level and albumin level. Charlson Comorbidity Index scoring was used to assess the comorbidity and severity of illness among the study cohort.[15] The McCabe score was used to assess the overall prognosis at the time of admission.[16] A limited activity of daily living score was created by combining Katz criteria[17] with the presence of urinary or bowel incontinence.

Low albumin was defined as level <3.4 g/dL anytime during the 60 days prior to CDI. Baseline creatinine was determined based on at least 2 preadmission readings during the last year prior to index admission. Follow-up phone calls with patients were conducted monthly for 1 year after index CDI date. Data obtained through follow-up calls combined with that obtained through patients' EMRs were used to collect information about clinical outcomes, including length of stay, recurrence of CDI, readmissions, and mortality rates. Recurrence of CDI was defined as recurrence of diarrhea or laboratory-confirmed CDI >2 weeks and ≤8 weeks after a patient's most recent laboratory-confirmed CDI.[12] Readmissions to our facility and other AHs were captured. Also, mortality rates within 1 year of the CDI date were captured for both cases and controls.

CDI classification

CDI was classified using the Society for Healthcare Epidemiology of America and the Infectious Diseases Society of America clinical practice guidelines for CDI in adults and the recommendations for surveillance of CDI.[12,18] Community-onset, acute health care–associated CDI was defined as a patient with CDI onset <48 hours after admission to our facility who was transferred directly from or exposed to an AH in the last 4 weeks prior to admission. Community-onset, LTCF-associated CDI was defined as a patient with disease onset <48 hours after admission to our facility who was a LTCF resident or was exposed to long-term care in the last 4 weeks and who had no history of acute care hospitalization during the last 12 weeks. Community-acquired or indeterminate (CA/I) CDI was defined as a patient presenting from home with disease onset <48 hours after admission to our facility and no history of health care exposure in the last 4 weeks prior to admission. Health care–onset, health care–associated, or hospital-acquired CDI was defined as CDI occurring after 48 hours of patient's admission to our facility.

Microbiologic testing of C difficile

Our microbiology laboratory used the ilumigene test (Meridian Bioscience, Cincinnati, OH) to check for *C difficile* in stool specimens. The illumigene *C difficile* test detects toxin A gene by loop-mediated isothermal amplification.[19]

Statistical analyses

IBM SPSS 22 (SPSS, Chicago, IL) was used for statistical analysis. Categorical variables were analyzed using the Fisher exact test. Student *t* test was used to compare the mean age of cases and controls. Mann-Whitney and Kruskal-Wallis tests were used to compare median values for continuous variables. The difference between the highest creatinine value (60 days prior to CDI) and the baseline creatinine value was calculated. Then the median difference was used as a cutoff point to create a categorical variable for the change in creatinine. Multivariate analysis was conducted using logistic regression. All variables included in the regression analysis were categorical except for age, which was continuous. Backward selection was performed to choose for independent predictors in the final model. Factors eliminated in the backward selection, but that still changed the β coefficient of potential predictors by ≥10%, were reentered into the model. A 2-way *P* value <.05 was considered significant.

RESULTS

There were 147 CDI patients admitted to our facility during the study period: 143 (97%) patients signed informed consent and agreed to participate in the study. The mean age of the entire cohort was 59 ± 17.93 years; 84 of the subjects (59%) were men, and 107 (75%) were black. Thirteen patients (9%) were classified as community-onset, acute health care–associated CDI, 17 patients (12%) were classified as community-onset LTCF-associated CDI, 47 patients (33%) were CA/I CDI, and 66 patients (46%) were hospital-acquired CDI (Fig 1). Of the 143 CDI patients admitted to our facility, 49 (34%) were discharged directly to LTCFs.

Risk factors associated with CDI patients with IFTs compared with those without IFTs

For the sake of the current study, 36 (30%) cases were compared with 84 (70%) controls. The mean age of CDI patients with