CONCISE COMMUNICATION

Community-Associated *Clostridium difficile* Infection among Veterans with Spinal Cord Injury and Disorder

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The impact of community-associated *Clostridium difficile* infection (CA-CDI) on patients with spinal cord injuries and disorders (SCI/Ds) is not fully understood. We examined CA-CDI cases among veterans with SCI/D, comparing them with community-onset, healthcare facility–associated (CO-HCFA) cases. Generally, patients with CA-CDI had less comorbidity, less severe CDI, and lower likelihood of antibiotic exposure.

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Clostridium difficile infection (CDI) is frequently characterized as an infection acquired in healthcare settings, but a significant proportion of cases develop in the community.[1] Multiple studies have found over 20% of CDI cases to be community associated.[2,3] Some findings also suggest that community-associated CDI (CA-CDI) cases may be increasing,[2] although a recent, population-based study from the Centers for Disease Control and Prevention found that 94% of cases were healthcare associated even though disease onset occurred outside of hospitals in 75% of cases.[4] These data point to a need for comprehensive surveillance[5] and deeper understanding of this segment of CDI.

The impact that increases in CA-CDI rates may have on patients with chronic and complex health needs, such as those with spinal cord injuries and disorders (SCI/Ds), is not fully understood, particularly because these patients often receive home-based healthcare outside of traditional clinical settings. Limited literature exists exploring the impact of community-associated infections in this population, and we have previously demonstrated that community-associated infections may be a predictor of hospital-acquired infections.[6]

The objectives of this study were to describe the incidence and risk factors for CA-CDI among patients with SCI/D and compare characteristics of CA-CDI with community-onset, healthcare facility–associated (CO-HCFA) cases.

METHODS

Study Design and Participants

In this retrospective cohort study, 8 years (January 1, 2002–December 31, 2009) of national Veterans Affairs (VA) medical data for veterans with SCI/D were examined. Data from 104 VA healthcare facilities (HCFs) with complete national data on patients with SCI/D were included. This study was approved by the Hines VA Institutional Review Board.

Definitions

Classifications of CDI cases, settings, mode of acquisition, and severity were defined by CDI surveillance recommendations[5] and published clinical practice guidelines for CDI.[7] We defined CO-HCFA CDI as cases occurring in VA HCFs within 48 hours of admission or visit, provided that the patient had been discharged from an HCF within the previous 4 weeks.[5,7] We identified CA-CDI as cases occurring in VA HCFs within 48 hours of admission or visit, provided that the patient had not been discharged from an HCF within the previous 12 weeks.[5,7] Indeterminate CDI cases were identified as occurring in VA HCFs within 48 hours of admission or visit, but in patients who had been discharged from an HCF within 4–12 weeks. Indeterminate cases were combined with CA-CDI cases in analyses because of similarities in characteristics.[8] The severity of illness definition for severe-complicated illness was modified to accommodate typical low blood pressure in patients with SCI/D; hypotension was defined for patients with paraplegia as systolic/diastolic less than 100/70 mm Hg and tetraplegia less than 90/60 mm Hg.[9]

Data Sources and Measures

Data were extracted from medical, pharmacy, and laboratory records from the following VA databases. The VA Emerging Pathogens Initiative Database was used to obtain *C. difficile* testing information. Demographic data and medical diagnoses before CDI onset were derived from VA inpatient and outpatient medical SAS databases. Blood pressure data were acquired from VA Corporate Data Warehouse; creatinine and white blood cell count information was obtained from VA Decision Support System (DSS) laboratory data to develop the severity of illness variable. Antibiotic exposure in the 6 weeks before CDI was extracted from VA DSS inpatient and outpatient pharmacy data. Measures for SCI/D injury level, date of onset, and etiology were obtained from VA Spinal Cord Dysfunction Registry data.

Analysis

Incidence was calculated per 10,000 patients with SCI/D treated each year instead of per 100,000 because of the size of the study population. Crude relationships between all var-

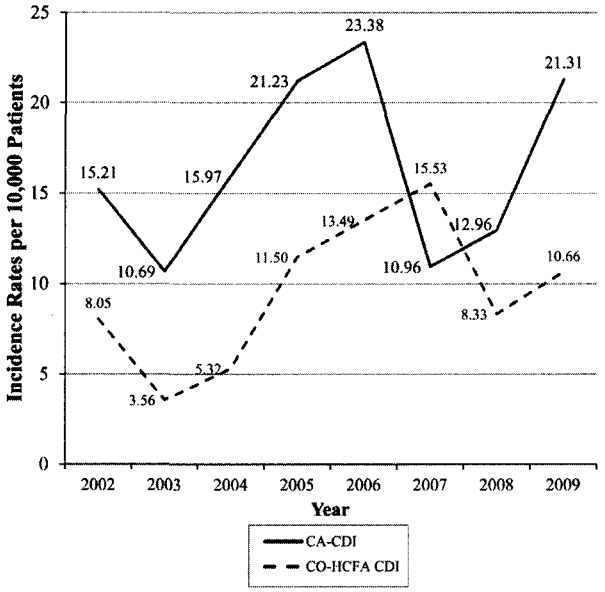

FIGURE 1. Incidence rates, per 10,000 patients, of community-associated *Clostridium difficile* infection (CA-CDI) and community-onset, healthcare facility–associated *C. difficile* infection (CO-HCFA CDI) among veterans with spinal cord injury and disorder, 2002–2009. CA-CDI incidence was 16.4 cases per 10,000 over the study period (global χ^2 P = .12).

iables and CA-CDI and CO-HCFA CDI were determined using unadjusted odds ratios. Cluster adjusted (within facility) logistic regression analyses were performed to further explore CA-CDI outcomes and compare with CO-HCFA cases. The final model included variables significant in bivariate analysis that remained significant in the model with P value less than or equal to .05. Statistical analyses were conducted using SAS software, version 9.3, and STATA MP software, version 12.1.

RESULTS

We identified 2,239 CDI cases in patients with SCI/D across the study period from inpatient, outpatient, and extended care data from the VA sites included for study. A total of 229 cases (10.2%) occurred in community settings; where 145 (63.3%) were CA-CDI and 84 (36.7%) were CO-HCFA cases. Among the CO-HCFA CDI cases, mean time (± standard deviation [SD]) to diagnosis of CDI after discharge from an HCF was 15.3 ± 7.8 days. Twenty-eight CA-CDI cases were classified as indeterminate but were similar to CA-CDI cases in patient demographic characteristics, severity, comorbidities, and proportion receiving antibiotics.[7] In comparing the analysis results with (1) indeterminate cases included with CA-CDI cases and (2) the indeterminate cases excluded (data not shown), we found no differences in the final adjusted model, except in macrolide exposure, which was no longer statistically significant when indeterminate cases were excluded. Thus, indeterminate cases were included in the CA-CDI group. Overall, 6.5% of cases (145 of 2,239) were CA-CDI. The CA-CDI cohort median age was 59 years, 97.9% of patients were male, nearly 85% were white, and approximately 52% of the cohort had paraplegia; the CO-HCFA cohort was similar.

The incidence of CA-CDI in our cohort was 16.4 cases per 10,000 patients and fluctuated annually over the study period, from 15.2 to 21.3 cases per 10,000 patients, although it was not statistically significant (global χ^2 P = .12; Figure 1). The incidence rate was typically higher in the CA-CDI cohort compared with the CO-HCFA CDI cohort (9.5 cases per 10,000 patients). CO-HCFA incidence rates varied over time with a moderate increase from 8.1 to 10.7 cases per 10,000 patients (P = .05). The CA-CDI cohort had less severe/severe complicated cases than did the CO-HCFA group (28.3% vs 42.9%; odds ratio [OR], 0.53 [95% confidence interval [CI], 0.30–0.92]).

Table 1 describes unadjusted and multivariable analyses assessing the association between characteristics and CDI onset (CA-CDI or CO-HCFA). The prevalence of several comorbidities was higher in the CO-HCFA group than in the CA-CDI group. In logistic regression analyses, the odds of aminoglycoside, third-generation cephalosporins, extended-spectrum penicillins, fluoroquinolones, macrolides, and proton pump inhibitor exposure was lower in patients with CA-CDI than in patients with CO-HCFA CDI. Additionally, the odds of having a pressure ulcer in the 30 days preceding CDI onset was lower among CA-CDI cases.

DISCUSSION

Veterans with SCI/D represent a unique population segment with complex, chronic needs. This is evident in that the proportion of CDI cases are predominately HCFA in this population; this is contrary to recent data showing that onset of 75% of HCFA CDI cases was outside of hospitals.[4] However, our findings on the proportion of CA-CDI cases, risk factors, and infection severity were generally consistent with other studies exploring CA-CDI in non-SCI/D populations.[2-4] Patients with CA-CDI had less comorbidity and fewer cases of severe CDI, compared to CO-HCFA cases. Pressure ulcers, although common in both groups, were more frequent among CO-HCFA cases, consistent with earlier research.[6] Additional examination is needed to understand the relationship between CA-CDI and other comorbidities.

Patients with CA-CDI were less likely to be exposed to antibiotics compared with patients with CO-HCFA. Earlier studies have found that over 30% of patients with CA-CDI had no recent exposure to antibiotics.[2,10] We were unable to identify recent antibiotic exposure in 46.2% of our CA-CDI sample. Thus, additional risk factors may exist for the SCI/D community. These data, although consistent with CA-CDI studies, are surprising considering the strong historical as-

TABLE 1. Bivariate Analysis of Risk Factors and Multivariable Logistic Regression Adjusted Odds Ratios (ORs) Comparing Community-Associated *Clostridium difficile* Infection (CA-CDI) and Community-Onset, Healthcare Facility–Associated *C. difficile* Infection (CO-HCFA CDI) Outcomes

Variable	CA-CDI (n = 145)	CO-HCFA CDI (n = 84)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Demographic and clinical characteristics				
Age, years				
18–49	27 (18.6)	9 (10.7)	Ref	...
50–64	70 (48.3)	41 (48.8)	0.57 (0.24–1.33)	...
≥65	48 (33.1)	34 (40.5)	0.47 (0.2–1.13)	...
Sex				
Male	142 (97.9)	82 (97.6)	1.15 (0.19–7.05)	...
Female	3 (2.1)	2 (2.4)	Ref	...
Race				
White	123 (84.8)	67 (79.8)	Ref	...
Black	15 (10.3)	14 (16.7)	0.58 (0.27–1.28)	...
Other	7 (4.8)	3 (3.6)	1.27 (0.32–5.08)	...
Region				
Northeast	28 (19.3)	20 (23.8)	Ref	...
Midwest	23 (15.9)	26 (31)	0.63 (0.28–1.41)	...
South	51 (35.2)	22 (26.2)	1.66 (0.77–3.54)	...
West	43 (29.7)	16 (19)	1.92 (0.85–4.32)	...
Duration of injury, years				
<5	39 (26.9)	20 (23.8)	Ref	...
5–11	21 (14.5)	11 (13.1)	0.98 (0.4–2.43)	...
11–16	8 (5.5)	5 (6)	0.82 (0.24–2.84)	...
≥16	64 (44.1)	37 (44)	0.89 (0.45–1.74)	...
Unknown	13 (9)	11 (13.1)	0.61 (0.23–1.59)	...
Level of injury				
Tetraplegia	69 (47.6)	31 (36.9)	Ref	...
Paraplegia	76 (52.4)	51 (60.7)	0.67 (0.39–1.16)	...
Unknown	0 (0)	2 (2.4)	0.09 (0–1.94)	...
Comorbidities with at least 10% prevalence[a]				
Within 30 days				
Any cardiovascular disease or disorder[b]	7 (4.8)	14 (16.7)	0.25 (0.10–0.66)	...
COPD	7 (4.8)	21 (25.0)	0.15 (0.06–0.38)	...
Diabetes	15 (10.3)	20 (23.8)	0.37 (0.18–0.77)	...
Pressure ulcer	24 (16.6)	28 (33.3)	0.4 (0.21–0.75)	0.24 (0.08–0.71)
Received diagnosis within study period				
Cancer	37 (25.5)	19 (22.6)	1.17 (0.62–2.21)	...
COPD	44 (30.3)	36 (42.9)	0.58 (0.33–1.02)	...
Any cardiovascular disease or disorder[b]	54 (37.2)	38 (45.2)	0.72 (0.42–1.24)	...
Diabetes	40 (27.6)	25 (29.8)	0.9 (0.5–1.63)	...
Liver disease	24 (16.6)	14 (16.7)	0.99 (0.48–2.04)	...
Pressure ulcer	79 (54.5)	49 (58.3)	0.85 (0.5–1.47)	...
Renal disease	22 (15.2)	12 (14.3)	1.07 (0.5–2.3)	...
Gastrointestinal ulcer	14 (9.7)	11 (13.1)	0.71 (0.31–1.64)	...
Medication exposure[c]				
Antibiotics within 6 weeks before CDI				
No	67 (46.2)	6 (7.1)	Ref	...
Yes	78 (53.8)	78 (92.9)	0.09 (0.04–0.22)	...
Aminoglycosides	2 (1.4)	11 (13.1)	0.09 (0.02–0.43)	...
Ampicillin	3 (2.1)	10 (11.9)	0.16 (0.04–0.59)	...
Amino-penicillin	17 (11.7)	12 (14.3)	0.8 (0.36–1.76)	0.05 (0.01–0.43)
Carbapenems	3 (2.1)	12 (14.3)	0.13 (0.03–0.46)	...
Clindamycin	5 (3.4)	12 (14.3)	0.21 (0.07–0.63)	...
Extended-spectrum penicillins	11 (7.6)	34 (40.5)	0.12 (0.06–0.26)	0.11 (0.03–0.37)
Fluoroquinolones	38 (26.2)	45 (53.6)	0.31 (0.17–0.54)	0.33 (0.14–0.79)
Third-generation cephalosporins	6 (4.1)	23 (27.4)	0.11 (0.04–0.3)	0.20 (0.06–0.71)
Macrolides	1 (0.7)	13 (15.5)	0.04 (0.0–0.3)	0.02 (0.001–0.44)

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TABLE 1 (*Continued*)

Variable	CA-CDI (n = 145)	CO-HCFA CDI (n = 84)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
PPI	48 (33.1)	48 (57.1)	0.37 (0.21–0.65)	0.33 (0.12–0.87)
Histamine 2 receptor antagonists	13 (9)	16 (19)	0.42 (0.19–0.92)	...
PPI or histamine 2 receptor antagonists	58 (40)	56 (66.7)	0.33 (0.19–0.58)	...

NOTE. Data are no. (%) of patients, unless otherwise indicated. CI, confidence interval; COPD, chronic obstructive pulmonary disease; PPI, proton pump inhibitor; Ref, reference.

[a] Compared with those without at least 10% prevalence.

[b] Includes congestive heart failure, cerebrovascular accident, myocardial infarction, and atherosclerotic peripheral vascular disease.

[c] Compared with those without exposure to that particular medication.

sociation of antibiotics with CDI. The role of antibiotic exposure as a CA-CDI risk factor requires additional study.

Study limitations include use of a laboratory-based definition to confirm CDI diagnosis rather than a clinical diagnosis of CDI symptoms. Additionally, analyses included only VA laboratory data and VA-prescribed antibiotics. We did not account for care or antibiotic treatment received outside of VA facilities. Consequently, this may have underestimated CDI rates and antibiotic exposure.

Effectively preventing CDI in communities requires a thorough understanding of the infection's impact. This study helps build our knowledge base, underscoring the need for additional research on the effects of CA-CDI on the SCI/D population.

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