CONCISE COMMUNICATION

The Epidemiology of Community *Clostridium difficile* Infection: A Five-Year Population-Based Study on the Bailiwick of Jersey, Channel Islands

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We studied healthcare-associated and community-associated *Clostridium difficile* infection (CDI) in Jersey, Channel Islands (2008–2012). The Island's stable population has reliable denominator data, a clearly defined at-risk population, and healthcare contact that is easily followed. The vast majority of CDI cases had had recent healthcare contact, and true community-associated disease is extremely rare.

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Reported rates of healthcare-associated *Clostridium difficile infection* (HA-CDI) are between 3 and 25 cases per 10,000 patient days.[1–3] In the community, published estimates of rates of CDI have been substantially lower at 8 to 25 cases per 100,000 person years, ~ 3,500-fold less than in hospitals,[4–8] but emerging reports suggest that the incidence of community-associated CDI (CA-CDI) is increasing. [9–13]

Patients may be discharged from the hospital and subsequently readmitted, so CA-CDI that truly originates in the community must be distinguished from cases of CDI that are related to a recent hospital admission, termed community-onset HA-CDI (COHA-CDI). This classification depends on the time period a CDI episode should be attributed to a recent inpatient stay, generally considered to be within 28 days, but there is a lack of consensus regarding how to categorize infection occurring 4–12 weeks after a hospital stay.[14] This uncertainty led to a classification of "unknown" cases for which it is unclear whether the infection is related to previous hospital admission or was acquired de novo in the community.

Estimating the incidence of CA-CDI may be imprecise because populations are mobile and catchment areas for specific healthcare institutions are not clearly set. Thus, most studies lack reliable estimates of denominator data of the size of the at-risk population.[8,10,15] Jersey, the largest of the Channel Islands and a British crown dependency, has a relatively stable, well-defined population of ~ 100,000 individuals, served by a single microbiology laboratory. We aimed to define the rate of CA-CDI, to assess the role of contact with hospitals and residents in long-term care facilities in these cases, and to present comparative data of the epidemiology of CA-CDI, COHA-CDI, and HA-CDI over 5 years, according to the classification proposed by the European Society of Microbiology and Infectious Diseases (ESCMID).[14]

MATERIALS AND METHODS

Design and Ethics

This study was approved by the hospital ethics board as part of an ongoing audit of CDI patients between January 2008 and November 2012. Data were collected from existing databases, with no impact on patient care.

Study Population

According to the 2011 population census, Jersey's resident population in March 2011 was 97,857.[16] The population is relatively stable, estimated as 97,200 and 99,000 at the ends of 2009 and 2012, respectively.

Clostridium difficile Diagnostic Methodology

Between 2008 and 2012, liquid stool samples were tested for *C. difficile* as previously described.[17] All patients with a positive CD toxin enzyme immunoassay (EIA) confirmed with a glutamate dehydrogenase (GDH) EIA were included in the study.

Data Collection

The infection control team in Jersey routinely tracks all cases of CDI in both the community and the single island hospital. In the community, the team is tasked with collating clinical information and stool samples and ensuring that appropriate infection control measures are instituted, under the guidance of a consultant microbiologist. Data on antibiotic prescription in the previous 28 days were gathered from drug charts. We also examined attendance at healthcare facilities in patients with CA-CDI, including outpatients, day surgery, and the renal dialysis center.

Case Definitions

Clostridium difficile infection (CDI) was defined as diarrhea with CD toxin positivity. Subsequent positive samples within 30 days of the initial positive sample were counted as part of the same episode.

The ESCMID guideline[14] was used to classify the origin of infection as follows:

1. Healthcare-associated infection (HA-CDI) is defined as CDI with symptom onset >48 hours after admission to a healthcare facility.

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2. Community onset, healthcare-associated infection (COHA-CDI) occurs in those with symptom-onset in the community within 28 days of discharge from a healthcare facility.
3. Community-associated infection (CA-CDI) refers to infection onset in the community with no prior admission to a healthcare facility for at least 84 days (12 weeks).
4. Unknown community-associated infection (UCA-CDI) relates to CDI occurring 4–12 weeks (28–84 days) after hospital admission; that is, the impact of antibiotic exposure or possible colonization with *C. difficile* related to that admission is unknown.

Cases admitted to the hospital <48 hours before symptom onset, having been admitted to hospital within the previous 4 weeks, were defined as COHA-CDI. The date of symptom onset was taken to be the date the first diarrhea sample was sent to the laboratory.

In our primary analysis, the definition of "healthcare facility" was restricted to the Jersey General Hospital. Nursing and residential homes were not considered as long-term healthcare facilities and instead were initially categorized as community associated. Subsequently, these cases were analyzed separately in a further evaluation of CA-CDI. Total hospital-bed occupancy was taken as the number of overnight stays in 2012, excluding pediatric and maternity beds. Patients with UCA-CDI who acquired the disease 4–12 weeks after discharge were analyzed separately and were counted as either CA-CDI or COHA-CDI in separate calculations to give a range of estimates. We used the publicly available Jersey census for age, gender, and population data.[16]

Statistical Analyses

Data were analyzed using Stata version 12 software (StataCorp, College Station, TX). The number of observations for each statistic and the analyses relied upon are presented in Table 1. Given the relatively stable Jersey population over the duration of the study, we calculated aggregated measures including the average incidence of cases in the population.

RESULTS

Between January 2008 and November 2012, 207 liquid stool samples were positive for CD toxin from a total of 4,506 samples tested (4.6%). In 2012, there were 55,736 overnight inpatient days, giving an estimated 274,053 inpatient days for the study period. This equates to testing rates of 164.4 samples tested per 10,000 inpatient days.

The biannual frequency of CDI during the study period is displayed in Figure 1, and the classification of these isolates into hospital or community-associated CDI is displayed in Figure 2. Overall, 139 patients (79%) had 1 positive sample, with 21% testing positive for CD toxin in a separate episode of the infection (at least 30 days after the first positive stool sample).

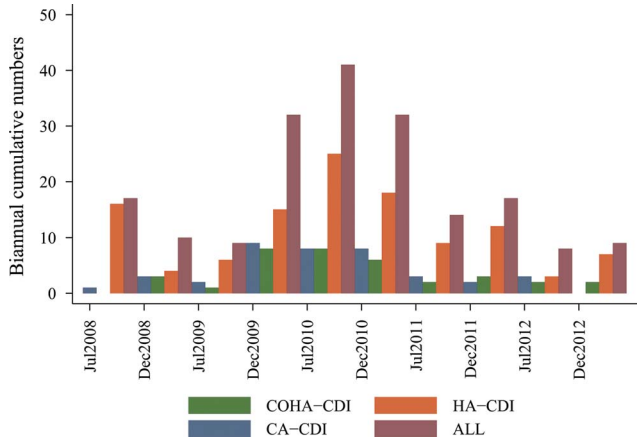

FIGURE 1. The biannual frequency of *Clostridium difficile* over the study period.
NOTE. HA-CDI, healthcare-associated *C. difficile* infection; COHA-CDI, community-onset healthcare-associated *C. difficile* infection; UCA-CDI, unknown community-associated *C. difficile* infection; CA-CDI, community-associated *C. difficile* infection.

Demographic, clinical and laboratory characteristics are presented by ESCMID subclassification in Table 1.

Incidence

Most infections (170 of 207, 82%) presented in the hospital (Table 1 and Figure 2). Most cases were HA-CDI (115 of 207, 56%) and COHA-CDI (39 of 207,19%), equating to an incidence of 4.2 and 1.4 cases per 10,000 patient days, respectively. The overall average hospital-associated disease incidence was 5.6 cases per 10,000 patient days.

In total, 39 of 92 of community-onset cases (42%) occurred within 28 days of discharge (COHA-CDI), and 18 of 92 (20%) occurred between 4 and 12 weeks (UCA-CDI). Also, CA-CDI was infrequent (35 of 207, 17% of cases), with an incidence of 7.27 cases per 100,000 person years. Of the 35 patients in the CA-CDI group, most had had contact with a healthcare facility. Moreover, 11 (31.4%) lived in residential or nursing homes (Table 1) and, of the remaining 24 individuals, 19 (54.3%) had clinical conditions requiring frequent visits to hospital such as renal dialysis or cancer chemotherapy patients, or outpatient contact within the preceding 90 days. Excluding these 30 patients, the estimated strictly defined CA-CDI with no recent contact with a healthcare facility, incidence was just 1.04 cases per 100,000 person years. We identified 19 cases of CA-CDI (25 including UCA-CDI) in the first half of the study and 16 cases (28 including UCA-CDI) in the second half of the study, with no detectable increase in the frequency of CA-CDI over this period.

DISCUSSION

The purpose of this population-based study of CDI on the Channel Island of Jersey was to define the incidence of CDI

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TABLE 1. Characteristics of Patients Presenting With *Clostridium difficile* Infection (CDI) Between 2008 and 2012

Summary Statistics		All Cases	HA-CDI	COHA-CDI	CA-CDI	UCA-CDI	Total Observations
Total patients*		176	101	33	29	13	176
Total episodes		207	115	39	35	18	207
Gender	F/M (%)	74/102	45/56	13/20	10/19	6/7	176
Age	Median (IQR)	79 (67–87)	79 (65–88)	80 (69–87)	80 (65–88)	70 (67–84)	
	Mean (SD)	76 (15)	76 (15)	76 (16)	77 (14)	75 (11)	
Residence	Home	118	75	22	13	8	
	Nursing/ Residential home	49	20	9	15	5	
	Residential Only	9	6	2	1	0	
CRP*	Median (IQR)	81 (36–187)	82 (36.5–175)	126 (42–205)	74 (31–191)	76.5 (28.5–216.5)	164
	Mean (SD)	112.3 (86.3)	109.3 (83.7)	124.7 (89.5)	106 (88.7)	117 (102)	
Albumin*	Median (IQR)	29 (25–33)	28 (23–32)	31 (26–35)	32 (28–35)	30 (23–35)	149
	Mean (SD)	29.4 (7.3)	28.1 (6.9)	20.6 (7.7)	32 (7.4)	30 (7)	
eGFR*	Median (IQR)	72 (43.5–100)	71 (44–100)	75 (35–100)	88 (54–100)	48 (24–100)	164
	Mean (SD)	67.4 (30.6)	67.7 (29.8)	64.3 (31.8)	75.3 (29.4)	55.5 (35)	
White cell count*	Median (IQR)	12.4 (8.8–17.1)	12.8 (8.8–17.8)	11.4 (7.6–16.6)	10.9 (9.6–13.8)	12.6 (9.5–17.7)	170
	Mean (SD)	14.6 (11.9)	15.2 (13.9)	14.4 (9.5)	12.6 (6.4)	14.7 (9.4)	
Exposure to antibiotics	No/total (%)	161/176	96/101	30/33	25/29	3/13	163
No. of antibiotics	Median (IQR)	2 (1–3)	2 (1–3)	2 (1–3)	1 (1–2)	2 (1–2)	176
Length of stay	Median (IQR)	25 (12–45)	37 (21–59)	10 (7–13)	12 (7–16)	9.5 (7.5–28.5)	152
	Mean (SD)	42.7 (92)	57.6 (109.9)	10 (6.3)	15 (14.1)	15 (12)	
Death within 30 days	No/total (%)	40/176 (22.7)	30/101 (29.7)	6/33 (18)	4/29 (13.8)	0/13	

NOTE. HA-CDI, healthcare-associated *C. difficile* infection; COHA-CDI, community-onset healthcare-associated *C. difficile* infection; UCA-CDI, unknown community-associated *C. difficile* infection; CA-CDI, community-associated *C. difficile* infection; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; SD, standard deviation; IQR, interquartile range.
*indicates the denominator is number of cases and not number of episodes.

relating to onset in healthcare or in the community. CA-CDI was uncommon, with an incidence of only 7.27 cases per 100,000 person years, similar to previous reports.[4–8] Using a stricter definition, where those living in nursing and/or residential homes or attending the hospital for chronic disease management were excluded from the analysis, CA-CDI incidence was just 1.04 per 100,000 person years. In our series, the 39 people in the COHA-CDI group represented ~25% of those who contracted infection in hospital.[13,18,19]

Over the past 20 years, HA-CDI has been a focus of attention, and hospitals have been regarded as the main reservoir of infection, with CA-CDI considered uncommon.[5,20,21] However, concerns have been raised by several population-based studies suggesting that the incidence of CDI in the community and in long-term care facilities is rising.[10,12,13,22] A US-based study found that 46% of CDI originated from nursing homes, 33% originated in the community, and only ~21% originated from hospitalized patients.[22] Similarly, a registry-based study from Finland indicated that CA-CDI accounted for one-third of CDI and that its incidence was increasing.[13] Reports suggest that CDI incidence in the community has reached levels comparable to those in healthcare facilities.[10] However, these studies may have overestimated the prevalence of CA-CDI, hindered by unreliable denominator data of the size of the at-risk population due to mobile populations, multiple microbiological laboratories, and no clear boundaries of the areas served by specific healthcare institutions.[8,10,15]

With its relatively stable population and dedicated microbiology facility, Jersey provided a serendipitous opportunity to study the current epidemiological trends of CDI in hospital, long-term care facilities and in the community. All stool samples were processed in 1 laboratory; a single routine infection control policy was in operation across long-term care facilities and the hospital; and the study was overseen by the same infection control team. These conditions ensured robust and comprehensive data, with no patients lost to follow-up.

Testing rates of 164.4 samples tested per 10,000 inpatient days were relatively high compared to rates reported elsewhere across Europe, so the low incidence of CA-CDI found in our study would be difficult to ascribe to undertesting.[23,24] Our findings are similar to those from a population-based study of active surveillance of 11 million people across 8 US states, in which 82% of 984 patients diagnosed with CA-CDI reported recent outpatient healthcare-facility exposure.[25] One-third of the patients in this report were lost to follow-up, potentially limiting its generalizability. We found CA-CDI to be relatively less severe,

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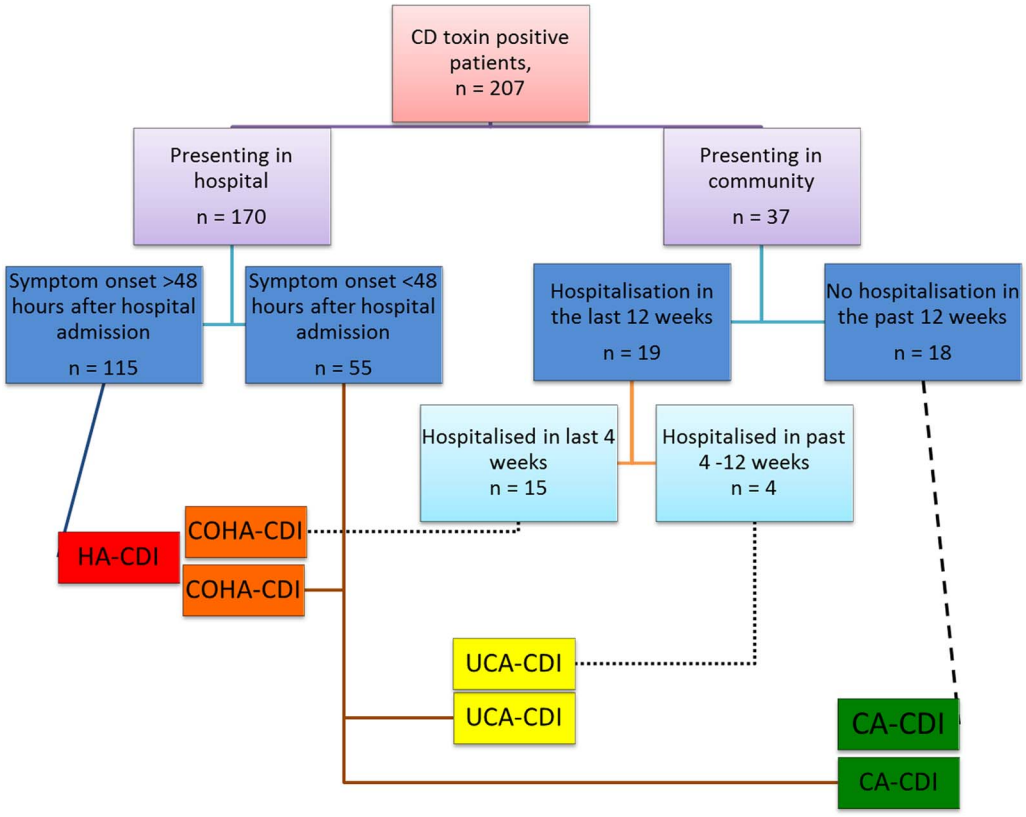

FIGURE 2. Classification of *Clostridium difficile* infection cases.
NOTE. HA-CDI, healthcare-associated *C. difficile* infection; COHA-CDI, community-onset healthcare-associated *C. difficile* infection; UCA-CDI, unknown community-associated *C. difficile* infection; CA-CDI, community-associated *C. difficile* infection.

supporting the findings of other observational studies,[12,13] possibly reflecting the variable virulence of differing ribotypes found in hospital and community settings.[13,18,19]

The case definition of "healthcare facility" used in most studies is synonymous with "hospital" and does not include nursing and/or residential homes. Although residence in these facilities has been associated with increased risk of CDI,[10] these cases are normally ascribed as CA-CDI. The definition of CA-CDI is of practical importance because knowing the epidemiology of CA-CDI is required to design effective infection control measures and to allocate resources to prevent spread. For these reasons, it is important to have clarity as to whether a typical case of CA-CDI occurs in patients with no hospital contact, who are best managed and targeted in primary care, or if efforts to control CA-CDI should focus on hospitals and long-term care facilities. Overly simplified case definitions may decrease the usefulness of national surveillance for CDI.

The limitations of this study include its retrospective design. Some cases of CDI may have gone undetected, especially mild, self-limiting disease. Other cases not captured in this study were those where empirical treatment was given without stool analysis in the community, although local guidelines discouraged this practice. In common with other studies, we have not actively sought cases of CDI but rather have relied upon counting the numbers of positive samples sent to a laboratory. Given the variability in the numbers of tests performed across Europe,[23] there may be an issue with case ascertainment and the numerator used in these estimates. Nevertheless, the testing rate of stool samples is relatively high compared to elsewhere in Europe, and the incidence of CDI in Jersey is similar to the European averages.[23]

In summary, our findings suggest that CDI is overwhelmingly linked to healthcare facilities and that exclusively community-associated disease is extremely rare, contributing little to the overall burden of disease. Most patients diagnosed outside the hospital environment had received antibiotics and had some prior association with healthcare facilities, either as inpatients or attending outpatient clinics where acquisition of infection was likely to have occurred. Infection control measures for CDI should focus on hospitals and long-term healthcare facilities because CDI is rare in patients who have no contact with healthcare facilities.

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