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Major Article

Correlation between hospital-onset and community-onset *Clostridioides difficile* infection incidence: Ward-level analysis following hospital relocation

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Keywords:
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Background: The development of hospital-onset *Clostridioides difficile* infection (HO-CDI) is affected by patient and environmental risk factors. We investigated changes in the incidence of HO-CDI after relocation to a newly built hospital with 50% private rooms and evaluated the associated factors.

Methods: A retrospective study was conducted to assess trends in CDI incidences before and after the relocation using segmented regression analysis model. The association between CDI incidence and environmental factors at the ward-level was assessed using a linear regression analyses model.

Results: The HO-CDI incidence decreased from 6.14 to 1.17 per 10,000 patient-days in the old and new hospital, respectively. Similarly, the community-onset CDI (CO-CDI) incidence decreased from 1.71 to 0.46 per 1000 admissions. HO-CDI incidence was positively correlated with CO-CDI incidence and inversely correlated with the private room ratio (adjusted R^2 = 0.83). Almost half of the CO-CDI patients had been hospitalized within 28 days preceding the onset.

Discussion: Environmental improvements after relocation may have reduced the reservoir of *C. difficile*, resulting in a decrease in the number of asymptomatic carriers and CO-CDI patients.

Conclusion: Relocation to a new hospital significantly reduced HO-CDI incidence, concomitantly decreasing the incidence of CO-CDI, potentially due to environmental improvements.

BACKGROUND

Clostridioides difficile (*C. difficile*) is a leading cause of nosocomial infections. It is a spore-forming anaerobic bacillus that is mainly transmitted through direct or indirect contact with infected patients and asymptomatic carriers.[1,2] Patients asymptomatically colonized by toxigenic strains may progress to *C. difficile* infection (CDI) during admission.[3] The most important risk factor for the development of CDI is exposure to antibiotic agents that suppress the normal bowel microbiota.[4,5] Brown et al.[6] reported that ward-level antibiotic prescribing was a risk factor for CDI, independent of the risk of antibiotic use in individual patients. Other commonly reported risk factors for CDI include advanced age, comorbidities (diabetes, renal failure, inflammatory bowel disease, and malignancy), use of proton pump inhibitors (PPIs) or non-steroidal anti-inflammatory drugs, gastrointestinal surgery, longer hospital stay, and exposure to healthcare settings.[2]

All patient beds at Okayama Saiseikai General Hospital (OSGH) (a teaching hospital in Okayama City, Japan) were relocated to a new hospital building located 200 m away on January 1st, 2016. We investigated whether the newly constructed environment changed the incidence of hospital-onset (HO)-CDI and evaluated several factors that could cause the change.

MATERIAL AND METHODS

OSGH is an acute care hospital with 553 beds and 15 departments, including internal medicine, surgery, orthopedics, obstetrics and gynecology, neurosurgery, urology, ophthalmology, dermatology, pediatrics, and palliative care departments. Approximately 50% of

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patients are admitted due to gastrointestinal (GI), hepatic, biliary, pancreatic, and respiratory diseases. In total, 1,500 new cases of cancer (eg, large intestine, stomach, lung, breast, and prostate) are treated each year. The outline of the hospital did not change before and after the relocation. There were no changes in the number of hospital staff (doctors, n = 163 ± 3; nurses, n = 535 ± 18) or criteria for hospital admission. While the total number of beds and wards also remained the same, the proportion of beds in private rooms increased from 27% to 51%, and the number of hand hygiene sinks increased from 607 to 960 places. Upon relocation, all inpatients at the old hospital were moved to the new hospital.

A retrospective study was conducted to compare the incidence of HO-CDI before and after hospital relocation and to assess several factors that influenced changes in incidence.

Throughout the study period, environmental decontamination and cleaning of patient rooms were conducted in the same manner. A specific protocol was followed for CDI prevention: (1) handwashing was recommended for patients and individuals who came into contact with infected patients, (2) protective gear was worn, (3) disinfectants were used, and (4) quarantine was implemented as required.

Definitions and categorization of patients

According to the clinical guidelines,[7] a CDI case was defined by the following criteria: diarrhea occurring ≥3 times a day or the presence of a toxic megacolon and stool samples testing positive for *C. difficile* toxins. TOX A/B QUIK CHEK (Nissui Pharmaceutical Co., Ltd., Tokyo, Japan) was used to assess the presence of *C. difficile* toxins between January and July 2013; *C. difficile* was confirmed by a positive result for toxins A and B. After August 2013, the *C. difficile* Quik Chek Complete test (Abbott Laboratories, Abbott Park, IL) was used, and the presence of *C. difficile* toxin was indicated by positive test results for both glutamate dehydrogenase and toxin B.

HO-CDI was defined by the onset of CDI at >72 hours after hospital admission, whereas community-onset (CO)-CDI was defined by the identification of CDI upon admission.

Furthermore, among cases of CO-CDI, those that developed in the community within 4 weeks of discharge from a healthcare facility were defined as community-onset, healthcare facility-associated CDI (CO-HCFA CDI).

CDI incidence analysis

HO-CDI and CO-CDI incidence rates were calculated as the number of cases per 10,000 patient-days and the number of cases per 1,000 admissions, respectively.

Quarterly CDI incidences were analyzed using a segmented regression model, including the timing of the hospital relocation. The study period was between January 1st, 2013, and June 30th, 2019, which was 3 years before and 3.5 years after the relocation, in order to effectively assess trends in CDI incidence. Subjects were inpatients aged ≥18 years who had been hospitalized for ≥72 hours across 26 wards (13 wards at each hospital, excluding the intensive care unit and pediatric ward).

Ward-level risk factor analysis

The intervention in this study was the hospital relocation and a change in the hospital environment. There was basically no change in patient characteristics before and after the relocation. Therefore, we focused on changes in environmental factors rather than changes in individual-level patient risk factors.

Since the transmission of *C. difficile* spores usually occurs in ward units, we investigated the relationship between environmental risk factors and HO-CDI incidence at the ward level. The ward-level analysis was performed for patients for the 2 years before (from January 1st, 2014, to December 31st, 2015) and after (from January 1st, 2016, to December 31st, 2017) the relocation. The following factors were assessed in each ward: proportion of private rooms, number of hand hygiene sinks per bed, number of inpatients, average patient age, PPI and antibiotic use by days of therapy (DOTs) per 100 patient-days, and number of CDI cases (further subdivided into HO-CDI and CO-CDI cases). The number of CO-CDI cases was incorporated to understand the impact of the environment. We identified the ward occupants for each inpatient day; when a patient was located in multiple wards on a given day, the patient was considered an occupant of the ward in which they were located at 12:00 PM.

All data were extracted (with patient identifiers removed) from the hospital administrative records. Ethics approval for this study was obtained from the OSGH Institutional Review Board (permission number: 190613 on 10th June 2019).

STATISTICAL ANALYSIS

Stata version 15 (StataCorp, College Station, TX) was used for the statistical analyses. We conducted an analysis using segmented regression model to estimate changes in quarterly incidence rates of CDI before and after hospital relocation. Outcomes were assessed by Poisson regression model and reported as the incidence rate ratio (IRR) comparing consecutive times using 95% confidence interval (CI). Chi-squared (χ^2) test was performed to compare the risk factors of individual patients in the old and new hospitals. Relationships between CDI incidence and ward-level variables were assessed by simple and multiple linear regression analyses models. Variance inflation factors (VIFs) were used to detect collinearity between variables. Correlation between HO-CDI incidence and CO-CDI incidence was determined using Spearman's rho test. The level of statistical significance for all tests was set at $P < .05$.

RESULTS

CDI incidence

We identified 322 HO-CDI cases in 524,475 patient-days (incidence of 6.14 cases per 10,000 patient-days) in the old hospital over the 3-year period and 62 HO-CDI cases in 531,697 patient-days (incidence of 1.17 cases per 10,000 patient-days) in the new hospital over the 3.5-year period. The quarterly trends of HO-CDI incidence rates over the 6.5-year period are shown in Figure 1A. Prior to the relocation, there was no downward trend (Coef. 0.005, 95% CI, −0.053 to 0.063, $P = .85$). After the relocation, there was a significant downward trend (Coef. −0.111, 95% CI, −0.185 to −0.038, $P = .006$), with the number of cases decreasing by 11% every 3 months. In the Poisson regression analysis, IRR was 0.19 (95% CI, 0.15-0.25, $P \leq .001$) around the time of hospital relocation, indicating a significant 81% reduction in HO-CDI cases at the new hospital. Moreover, this decline was not transient, but continued for at least 3.5 years after the relocation.

Similarly, the quarterly trends of CO-CDI incidence over the 6.5-year period are shown in Figure 1B. We identified 63 CO-CDI cases in 36,921 admissions (incidence of 1.71 cases per 1,000 admissions) in the old hospital and 20 CO-CDI cases in 43,826 patient-admissions (incidence of 0.46 cases per 1,000 admissions) in the new hospital. In the Poisson regression analysis, IRR was 0.27 (95% CI, 0.16-0.44, $P < .001$) around the time of hospital relocation. There was no significant downward trend before relocation (Coef. −0.006, 95% CI, −0.086 to 0.073, $P = .87$).

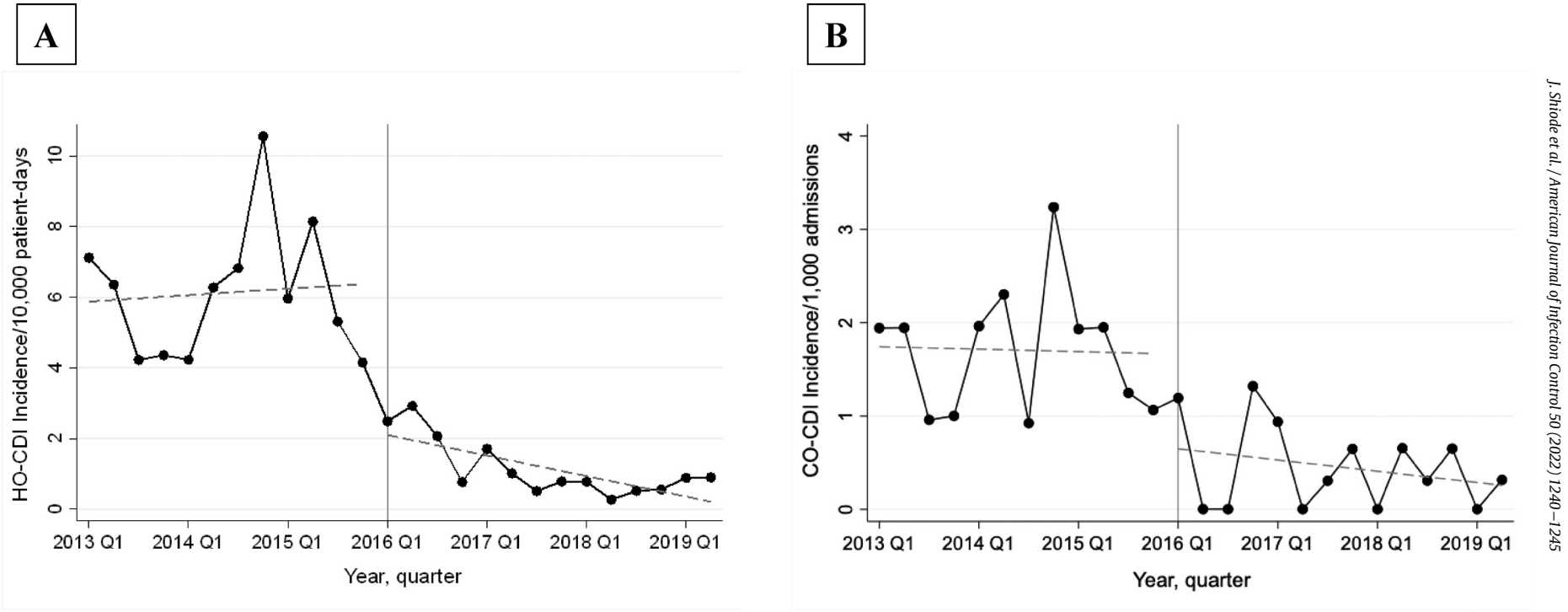

Fig 1. Quarterly *Clostridioides difficile* infection (CDI) incidence before and after hospital relocation. (**A**) hospital-onset CDI (HO-CDI) incidence. (**B**) community-onset CDI (CO-CDI) incidence. The vertical lines indicate the day of hospital relocation.

General comparison between the 2 hospitals

Over the 2-yearly periods, we identified 222 HO-CDI cases out of 19,323 inpatients in the old hospital and 48 HO-CDI cases out of 19,268 inpatients in the new hospital.

Compared to the old hospital, the number of patients aged ≥75 years (P = .04) and those receiving cephalosporins (P = .045) increased, and the number of patients receiving PPIs (P < .001), carbapenems (P < .001), fluoroquinolones (P < .001), or clindamycin (P < .001) decreased in the new hospital (Table 1).

In terms of the facilities, the new hospital had a greater proportion of private rooms (51%, 277 rooms) compared to the old hospital (27%, 148 rooms).

Furthermore, the new hospital had a greater number of hand hygiene sinks per bed (1.7 vs 1.1). In the old hospital, the numbers of HO-CDI cases per 10,000 patient-days in private rooms and shared rooms were 6.53 and 6.44, respectively. The corresponding values in the private and shared rooms in the new hospital were 1.1 and 1.7, respectively. When combining the results of both hospitals, the risk ratio of HO-CDI incidence in private rooms compared to shared rooms was 0.71 (95% CI, 0.54-0.92). In total, 45 CO-CDI cases were documented at the old hospital, while 14 cases were recorded in the new hospital. Approximately half of those cases (26 and 3 cases in the old and new hospitals, respectively) included patients who had developed CDI within 4 weeks of hospital discharge.

Ward-level analysis

An overview of the ward-level characteristics and CDI incidence among the combined total of 26 wards from both hospitals is shown in Table 2. While there was only one ward in the old hospital in which the majority (≥50%) of beds were in private rooms, the new hospital had 11 such wards. The number of hand hygiene sinks per bed was also higher in the new hospital.

Among the 26 wards, eight wards (obstetrics and gynecology, ophthalmology, neurosurgery, and palliative care unit) had no cases of CO-CDI. In those wards, the average incidence of HO-CDI was very low (0.23 cases per 10,000 patient-days).

Simple linear regression analysis of risk factors affecting HO-CDI incidence revealed a positive correlation with CO-CDI incidence, PPI DOTs, and carbapenem DOTs. In addition, negative correlations with the proportion of private rooms and number of hand hygiene sinks per bed were found (Table 3). The number of hand hygiene sinks increased with the increase in the number of private rooms. The VIF indicated significant collinearity between these variables (VIF = 6.02); therefore, we removed the 'hand hygiene sinks' variable from the model. According to the multiple linear regression analysis, CO-CDI incidence was positively correlated and the proportion of private rooms was negatively correlated with HO-CDI incidence (adjusted R^2 = 0.83).

The incidence of CO-CDI was the strongest predictor of HO-CDI incidence (Fig 2). Each CO-CDI case increase per 1,000 admissions was associated with 2.1 HO-CDI cases increase per 10,000 patient-days (P < .001, R^2 = 0.73).

Table 1
Comparison of hospital characteristics and inpatient demographic data

	Old hospital	New hospital	*P*-value
Total beds	553	553	
Number of private rooms	148	277	
Hand hygiene sinks per bed	1.1	1.7	<.001
Inpatients	19323	19268	
Male/female	10086/9237	10028/9240	.765
Age at admission, years, mean ± SD	68.3 ± 17.3	68.7 ± 17.3	.092
Age over 75 years	8128	8304	.04
Medication			
Proton pump inhibitors	8151	7460	<.001
Carbapenems	1673	1253	<.001
Cephalosporins	11353	11514	.045
Penicillin compounds	1911	1908	.967
Fluoroquinolones	1824	1573	<.001
Clindamycin	185	117	<.001
Hospital-onset CDI patients	222	48	<.001
Incidence per 10,000 patient-days	6.45	1.53	<.001
in private room	6.53	1.10	
in shared room	6.44	1.70	
Community-onset CDI patients	45	14	<.001
Incidence per 1,000 admissions	1.81	0.56	<.001
Community-onset HCFA patients	33	10	
Patients re-admitted within 4 weeks	26	3	

CDI, *Clostridioides difficile* infection; HCFA, healthcare facility associated; SD, standard deviation.

DISCUSSION

Previous studies have reported HO-CDI incidence rates ranging from 2.5 to 10.1 cases per 10,000 patient-days in Western countries[7,8] and 0.8 to 5.7 cases per 10,000 patient-days in Japan.[9,10] In the present study, incidence rates of HO-CDI at OSGH decreased from 6.14 to 1.17 cases per 10,000 patient-days following relocation. To determine the reason for this decline, we compared the potential risk factors for HO-CDI between the two hospital settings. As the large reduction in CDI incidence following relocation could not be explained by differences in individual-level patient risk factors, we considered the potential effects of environmental factors. The transmission of *C. difficile* is thought to be due to the contamination of the hospital rooms or the hands of healthcare staff.[11] As the range of activities performed by the healthcare staff and patients was typically limited to within the wards, an analysis of risk factors at the ward-level was performed. Our findings revealed that HO-CDI incidence was correlated with two significant factors and one suggestive factor: CO-CDI incidence rate (P = .004), proportion of private rooms (P = .018), and carbapenem use (P = .068). Regarding antibiotic administration within hospital wards, Brown et al.[6] reported a significant relationship between CDI incidence and DOTs per 100 patient-days. Although Kipnis et al.[12] could not identify any risk factor associated with individual patients, days of antibiotic therapy in the ward (particularly third-generation cephalosporins) was a significant risk factor. In the present study, carbapenem was the only antibiotic type that showed a correlation with HO-CDI incidence.

We found that the proportion of private rooms was inversely correlated with HO-CDI incidence. This result differs from that reported by Darley et al.,[13] who did not find a significant difference in HO-CDI incidence following relocation to a new hospital, in which 75% of the hospital rooms were private. A similar observation was reported by McDonald et al.,[14] who assessed CDI incidence following relocation to a new hospital in which all rooms were private. In contrast, another study reported a decrease in HO-CDI incidence following a 100% conversion to private rooms.[15]

In the present study, the incidence of CO-CDI was the most significant factor for HO-CDI incidence. Curry et al. used multilocus variable number tandem repeat analysis genotyping and concluded that 29% of the 56 incident CDI cases could be linked to asymptomatic carriers.[16] Furthermore, as reported in a cohort study by Kong et al., who used whole-genome sequencing, 32% of 201 CDI cases were linked to both infected and asymptomatic carriers,[17] and being an asymptomatic carrier may be associated with the incidence of HO-CDI. These findings may be attributed to the contamination of the hospital wards due to the hospitalization of CO-CDI patients, which would result in the creation of a reservoir of *C. difficile* and a subsequent increase in HO-CDI cases. *C. difficile* spores can persist in the environment for up to 5 months and can be isolated from beds, floors, and walls in hospital facilities that

Table 2
Variation in ward-level characteristics and *Clostridioides difficile* infection incidence

	A Old hospital												
	Old Hospital Ward												
Variable	1	2	3	4	5	6	7	8	9	10	11	12	13
Environmental factors													
Proportion of private rooms (%)	52.0	45.5	37.5	37.5	37.5	36.2	24.1	18.6	17.0	17.0	13.0	8.9	0.0
Hand hygiene sinks per bed	1.60	1.79	1.38	1.31	1.33	1.36	1.45	0.74	0.66	0.66	0.65	0.60	0.90
Community-onset CDI patients	0	0	6	3	4	6	0	6	5	1	1	4	4
Incidence per 1,000 admissions	0.0	0.0	3.7	1.3	2.2	3.4	0.0	3.6	3.0	0.6	0.8	3.0	7.2
Patient-days, in thousands	10.4	13.3	31.6	28.4	29.4	30.6	20.6	30.1	33.7	30.7	27.4	27.9	13.8
Patient mean age, years	75.9	52.0	73.6	67.4	66.4	71.4	70.3	72.4	70.7	67.9	67.1	68.4	74.4
Medication DOTs per 100 PD													
Proton pump inhibitors	29.8	13.1	34.6	22.5	16.2	40.0	18.4	41.3	35.4	17.2	26.6	23.6	40.3
Carbapenems	3.6	1.1	7.4	4.6	3.5	5.4	2.6	6.6	6.7	3.0	2.7	2.1	6.7
Cephalosporins	7.1	18.6	12.3	23.1	17.2	15.7	25.8	13.6	11.1	15.4	19.6	22.0	14.2
Penicillin compounds	3.5	2.4	8.1	3.3	1.7	3.9	2.5	6.0	6.4	2.3	2.4	2.2	4.5
Fluoroquinolones	1.8	1.2	3.2	3.6	2.0	2.6	1.3	3.0	2.2	2.2	2.9	1.9	2.3
Clindamycin	0.0	0.2	0.4	1.2	0.2	0.6	0.1	0.1	0.5	0.3	0.6	0.3	0.5
Hospital-onset CDI patients	0	0	38	19	12	25	2	33	25	22	13	8	21
Incidence per 10,000 PD	0.0	0.0	12.0	6.7	4.1	8.2	1.0	11.0	7.4	7.2	4.7	2.9	15.2
	B New hospital												
	New Hospital Ward												
Variable	14	15	16	17	18	19	20	21	22	23	24	25	26
Environmental factors													
Proportion of private rooms (%)	68.0	59.0	54.3	52.4	52.4	52.4	52.4	52.4	52.4	50.0	50.0	42.9	42.9
Hand hygiene sinks per bed	2.36	1.56	2.06	1.76	1.67	1.67	1.79	1.74	1.76	2.38	2.13	1.60	1.48
Community-onset CDI patients	0	4	0	2	3	1	1	0	0	2	0	2	1
Incidence per 1,000 admissions	0.0	2.5	0.0	1.4	1.8	0.7	0.6	0.0	0.0	2.5	0.0	1.3	0.5
Patient-days, in thousands	11.9	25.9	17.2	25.3	26.4	25.5	26.6	24.7	26.1	15.4	14.1	25.9	27.6
Patient mean age, years	75.4	70.0	67.8	69.2	72.5	69.0	67.9	72.0	66.9	71.1	51.9	73.0	72.5
Medication DOTs per 100 PD													
Proton pump inhibitors	37.7	31.8	14.3	23.6	32.0	20.5	17.7	19.8	16.4	41.9	14.9	37.0	35.0
Carbapenems	3.2	4.8	3.6	2.0	5.5	2.2	3.6	2.5	3.2	4.6	2.0	5.5	5.0
Cephalosporins	8.5	13.4	35.7	19.6	12.1	18.8	18.2	29.1	18.9	18.2	19.6	15.4	19.2
Penicillin compounds	3.4	5.1	4.0	3.4	8.2	3.9	3.2	3.4	3.0	5.6	2.6	7.1	4.4
Fluoroquinolones	2.2	1.7	2.3	1.9	2.8	2.1	2.8	2.6	2.7	2.7	1.4	3.2	2.5
Clindamycin	0.0	0.2	1.4	0.8	0.1	1.4	0.2	0.7	0.1	0.5	0.2	0.3	0.1
Hospital-onset CDI patients	0	8	0	6	6	2	1	1	1	3	0	7	4
Incidence per 10,000 PD	0.0	3.1	0.0	2.4	2.3	0.8	0.4	0.4	0.4	1.9	0.0	2.7	1.5

CDI, *Clostridioides difficile* infection; DOTs, days of therapy; PD, patient-days.

were previously used by patients with CDI.[18] In the newly built hospital, these environmental contaminations had been cleaned up, and the reservoir of *C. difficile* had disappeared. Therefore, relocation to the new hospital had reduced the number of asymptomatic carriers and incidence of CO-CDI. However, the fact that the decline in incidence continued for over 3.5 years cannot be explained only by the new facilities. The increased number of private rooms and hand hygiene sinks may contribute to environmental improvement. The CDI incidence in a hospital is usually related to the incidence of CDI in the wider community. Although we did not investigate the CDI rates in the wider community, the sharp downward trend in CO-CDI incidence is thought to reflect relocation rather than the natural decrease in CDI incidence in the community.

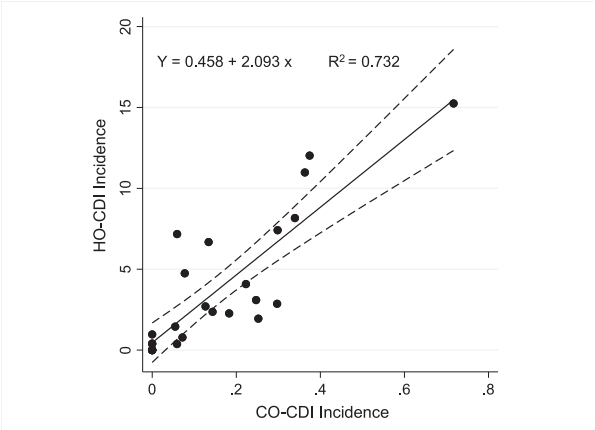

Fig 2. Correlation between hospital-onset (HO) and community-onset *Clostridioides difficile* infection (CO-CDI) incidence.

In the new hospital, reduced risks of environmental contamination would have resulted in a decline in the number of asymptomatic carriers, thus eliminating the vicious circle of recontamination and transmission in patients with CDI. Our observation of a gradual decline in HO-CDI incidence over a few months after the relocation suggests that it was not necessarily the new facilities that had a direct effect on the reduction of infection, but rather the interruption of the chain of events that led to the initial generation of CO-CDI cases.

Approximately half of the CO-CDI patients in OSGH hospital were re-admitted within 28 days, which seems to play an important role in this chain of events. If most CO-CDI patients comprised patients from other medical institutions or welfare facilities, the number of patients with CO-CDI would not have decreased even after relocation, and the number of HO-CDI patients would not have decreased significantly.

Table 3
Ward-level risk factors for hospital-onset *Clostridioides difficile* infection incidence density assesed by simple and multiple linear regression analyses

	Simple linear regression analysis				Multiple linear regression analysis			
Variable	β-Coefficient	95% CI		*P*-value	β-Coefficient	95% CI		*P*-value
Community-onset CDI incidence	2.09	1.56	to 2.63	< 0.001	1.21	0.43	to 1.99	0.004
Proportion of private rooms	−16.50	−23.79	to −9.21	< 0.001	−7.17	−12.94	to −1.39	0.018
Hand hygiene sinks per bed	−5.31	−7.94	to −2.68	< 0.001				
Mean age	0.23	−0.06	to 0.52	0.120	−0.04	−0.22	to 0.14	0.649
Proton pump inhibitor DOTs per 100 PD	0.22	0.07	to 0.38	0.007	−0.07	−0.22	to 0.08	0.331
Carbapenems DOTs per 100 PD	1.75	1.04	to 2.46	< 0.001	1.02	−0.08	to 2.12	0.068
Cephalosporins DOTs per 100 PD	−0.22	−0.49	to 0.05	0.107	−0.09	−0.24	to 0.06	0.242
Penicillin compounds DOTs per 100 PD	0.84	−0.07	to 1.75	0.070	−0.37	−1.14	to 0.41	0.332
Fluoroquinolones DOTs per 100 PD	2.64	−0.04	to 5.33	0.054	1.21	−0.42	to 2.83	0.137
Clindamycin DOTs per 100 PD	0.39	−4.1	to 4.88	0.859				

CDI, *Clostridioides difficile* infection; CI, confidence interval; DOTs, days of therapy; PD, patient-days.

Future studies should consider the use of DNA sequence analysis and molecular typing of *C. difficile* isolates to facilitate a more accurate understanding of how transmissions occur.

The present study had some limitations. First, we only included patients at a single hospital, and there was an insufficient number of wards (n = 26) for a widely applicable ward-level analysis. Second, we could only speculate about the relationship between HO-CDI and CO-CDI cases with potential transmission, as no genetic testing of *C. difficile* isolates was performed.

CONCLUSIONS

The intervention of hospital relocation resulted in a marked decline of HO-CDI incidence (IRR 0.19). Similarly, the CO-CDI incidence also decreased after the relocation (IRR 0.27). Ward-level analysis revealed that the HO-CDI incidence rate was significantly correlated with the CO-CDI incidence rate and proportion of private rooms. Environmental improvements, including new facilities and increased proportion of private rooms, are considered to be associated with lower CO-CDI incidence and a subsequent decrease in the HO-CDI incidence. The fact that almost half of the CO-CDI cases consist of patients re-admitted within 28 days after discharge seems to have contributed to the decrease in CO-CDI cases.

AUTHOR CONTRIBUTION

JS, MF, and JN were responsible for the study concept and design. MI, SI, AF, and MY acquired the data. JS and MF cleaned the data and performed statistical analysis. JS prepared the manuscript. JS and MF helped with data interpretation and manuscript review. All authors read and approved the final manuscript.

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