J Korean Med Sci. 2024 Apr 1;39(12):e118
https://doi.org/10.3346/jkms.2024.39.e118
eISSN 1598-6357·pISSN 1011-8934

JKMS

Original Article
Infectious Diseases



# Incidence of *Clostridioides difficile* Infections in Republic of Korea: A Prospective Study With Active Surveillance vs. National Data From Health Insurance Review & Assessment Service



**Received:** Sep 26, 2023
**Accepted:** Feb 14, 2024
**Published online:** Mar 18, 2024

**Address for Correspondence:**
**Hyunjoo Pai, MD, PhD**
Division of Infectious Disease, Department of Internal Medicine, Hanyang University College of Medicine, 222 Wangsimni-ro, Seongdong-gu, Seoul 04763, Korea.
Email: paihj@hanyang.ac.kr
paihyunjoo@gmail.com



**ORCID iDs**
Jieun Kim
https://orcid.org/0000-0002-6214-3889
Rangmi Myung
https://orcid.org/0000-0002-5776-1009
Bongyoung Kim
https://orcid.org/0000-0002-5029-6597
Jinyeong Kim
https://orcid.org/0000-0002-2360-7038
Tark Kim
https://orcid.org/0000-0002-8829-4183
Mi Suk Lee
https://orcid.org/0000-0001-8951-5032
Uh Jin Kim
https://orcid.org/0000-0002-8463-6297
Dae Won Park
https://orcid.org/0000-0002-7653-686X

**Jieun Kim**,[1] **Rangmi Myung**,[2] **Bongyoung Kim**,[1] **Jinyeong Kim**,[3] **Tark Kim**,[4] **Mi Suk Lee**,[5] **Uh Jin Kim**,[6] **Dae Won Park**,[7] **Yeon-Sook Kim**,[8] **Chang-Seop Lee**,[9] **Eu Suk Kim**,[10] **Sun Hee Lee**,[11] **Hyun-Ha Chang**,[12] **Seung Soon Lee**,[13] **Se Yoon Park**,[1] **Hee Jung Choi**,[14] **Hye In Kim**,[15] **Young Eun Ha**,[16] **Yu Mi Wi**,[17] **Sungim Choi**,[18] **So Youn Shin**,[19] **and Hyunjoo Pai**[1]

[1]Department of Internal Medicine, Hanyang University College of Medicine, Seoul, Korea
[2]Department of Non-benefits Management, National Health Insurance Service, Wonju, Korea
[3]Hanyang University Guri Hospital, Guri, Korea
[4]Divison of Infectious Diseases, Department of Internal Medicine, Soonchunhyang University Bucheon Hospital, Bucheon, Korea
[5]Department of Internal Medicine, Kyung Hee University College of Medicine, Seoul, Korea
[6]Department of Infectious Diseases, Chonnam National University Medical School, Gwangju, Korea
[7]Division of Infectious Diseases, Department of Internal Medicine, Korea University Ansan Hospital, Ansan, Korea
[8]Division of Infectious Diseases, Chungnam National University School of Medicine, Daejeon, Korea
[9]Department of Internal Medicine and Research Institute of Clinical Medicine, Jeonbuk National University Medical School and Hospital, Jeonju, Korea
[10]Department of Internal Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Korea
[11]Department of Internal Medicine, Pusan National University School of Medicine, Busan, Korea
[12]Division of Infectious Diseases, Department of Internal Medicine, School of Medicine, Kyungpook National University, Daegu, Korea
[13]Division of Infectious Diseases, Department of Internal Medicine, Hallym University, Chuncheon Sacred Heart Hospital, Hallym University College of Medicine, Chuncheon, Korea
[14]Department of Internal Medicine, Ewha Womans University College of Medicine, Seoul, Korea
[15]Department of Infectious Diseases, Daegu Fatima Hospital, Daegu, Korea
[16]Department of Infectious Diseases, Bucheon Sejong Hospital, Bucheon, Korea
[17]Division of Infectious Diseases, Samsung Changwon Hospital, Sungkyunkwan University, Changwon, Korea
[18]Division of Infectious Diseases, Dongguk University Ilsan Hospital, Goyang, Korea
[19]Department of Infectious Diseases, International St. Mary's Hospital, Catholic Kwandong University College of Medicine, Incheon, Korea

## ABSTRACT

**Background:** Since the emergence of hypervirulent strains of *Clostridioides difficile*, the incidence of *C. difficile* infections (CDI) has increased significantly.
**Methods:** To assess the incidence of CDI in Korea, we conducted a prospective multicentre observational study from October 2020 to October 2021. Additionally, we calculated the incidence of CDI from mass data obtained from the Health Insurance Review and Assessment Service (HIRA) from 2008 to 2020.

Yeon-Sook Kim
https://orcid.org/0000-0003-1142-5488
Chang-Seop Lee
https://orcid.org/0000-0002-2897-2202
Eu Suk Kim
https://orcid.org/0000-0001-7132-0157
Sun Hee Lee
https://orcid.org/0000-0003-2093-3628
Hyun-Ha Chang
https://orcid.org/0000-0002-9405-2121
Seung Soon Lee
https://orcid.org/0000-0003-1797-3426
Se Yoon Park
https://orcid.org/0000-0002-4538-7371
Hee Jung Choi
https://orcid.org/0000-0002-1468-4074
Hye In Kim
https://orcid.org/0000-0001-7162-4150
Young Eun Ha
https://orcid.org/0000-0001-5213-7082
Yu Mi Wi
https://orcid.org/0000-0003-3625-3328
Sungim Choi
https://orcid.org/0000-0001-8692-5570
So Youn Shin
https://orcid.org/0000-0002-4242-2805
Hyunjoo Pai
https://orcid.org/0000-0003-4143-035X

**Funding**

This research was supported by a grant (2020-ER5409-00) from the Research of the Korea Centers for Disease Control and Prevention, and a Pfizer grant (60340919). The funders had no role in the study design, data collection and interpretation, or decision to submit this manuscript for publication.

**Disclosure**

The authors have no potential conflicts of interest to disclose.

**Author Contributions**

Conceptualization: Kim J, Pai H. Data curation: Kim J, Myung R. Formal analysis: Kim J, Myung R. Investigation: Kim B, Kim J, Kim T, Lee MS, Kim UJ, Park DW, Kim YS, Lee CS, Kim ES, Lee SH, Chang HH, Lee SS, Park SY, Choi HJ, Kim HI, Ha YE, Wi YM, Choi S, Shin SY. Methodology: Kim J, Kim B, Kim J, Pai H. Software: Kim J, Myung R. Validation: Kim J, Myung R, Pai H. Writing - original draft: Kim J, Pai H. Writing - review & editing: Kim J, Myung R, Kim B, Kim J, Kim T, Lee MS, Kim UJ, Park DW, Kim YS, Lee CS, Kim ES, Lee SH, Chang HH, Lee SS, Park SY, Choi HJ, Kim HI, Ha YE, Wi YM, Choi S, Shin SY, Pai H.

**Results:** In the prospective study with active surveillance, 30,212 patients had diarrhoea and 907 patients were diagnosed with CDI over 1,288,571 patient-days and 193,264 admissions in 18 participating hospitals during 3 months of study period; the CDI per 10,000 patient-days was 7.04 and the CDI per 1,000 admission was 4.69. The incidence of CDI was higher in general hospitals than in tertiary hospitals: 6.38 per 10,000 patient-days (range: 3.25–12.05) and 4.18 per 1,000 admissions (range: 1.92–8.59) in 11 tertiary hospitals, vs. 9.45 per 10,000 patient-days (range: 5.68–13.90) and 6.73 per 1,000 admissions (range: 3.18–15.85) in seven general hospitals. With regard to HIRA data, the incidence of CDI in all hospitals has been increasing over the 13-year-period: from 0.3 to 1.8 per 10,000 patient-days, 0.3 to 1.6 per 1,000 admissions, and 6.9 to 56.9 per 100,000 population, respectively.
**Conclusion:** The incidence of CDI in Korea has been gradually increasing, and its recent value is as high as that in the United State and Europe. CDI is underestimated, particularly in general hospitals in Korea.

**Keywords:** *Clostridioides difficile* Infection; Incidence; Active Surveillance; Big Data

## INTRODUCTION

Since the emergence of hypervirulent strains of *Clostridioides difficile*, the incidence of *C. difficile* infections (CDI) has increased significantly, particularly in North America and Europe.[1] In 2013, the Centers for Disease Control and Prevention (CDC) announced CDI as a major threat to the United States (U.S.). For the effective management of CDI in hospitals, guidelines recommend implementing surveillance of CDI rates and providing feedback to hospitals or wards, especially during endemic and outbreak situations.[2]

The incidence of CDI varies among countries.[3] In the United State, according to a meta-analysis conducted from 2010 to 2019, the hospital-onset CDI incidence rate was 8.3 cases per 10,000 patient-days.[4] In contrast, a meta-analysis showed that, compared to that of the US or Europe, Asian countries had a lower CDI incidence rate of 5.3 per 10,000 patient-days.[5] In retrospective studies conducted in Korea, the incidence of CDI ranged from 1.7 per 1,000 admissions in 2004 to 2.7 per 1,000 admissions in 2008.[6,7] However, in studies involving active surveillance, the incidence of CDI ranged from 2.7 to 7.16 per 10,000 patient days in 2011–2012[8] and 2009,[9] respectively. These findings indicate that the incidence of CDI varies according to the institution and the surveillance program in place.

The risk factors contributing to the development of CDI include antibiotic use, advanced age, and hospitalization.[10] Despite experiencing a decrease of −0.3% in expenditure from 2011 to 2020, Korea still ranks third among the 17 Organisation for Economic Co-operation and Development (OECD) countries in terms of expenditure on the Anatomical Therapeutic Chemical Classification System (ATC code J, which are anti-infectives for systemic use.[11] Furthermore, by 2025, Korea is expected to enter a super-aged society, with a rapid increase in the older person population, accounting for 20.6% of the total population.[12] Therefore, the incidence of CDI is expected to continue to increase.

To assess the current incidence of CDI in Korea, we conducted a prospective multicentre observational study using a similar active surveillance program in 18 hospitals across the Korean Peninsula. Additionally, we calculated the incidence of CDI from mass data obtained from the Health Insurance Review and Assessment Service (HIRA) from 2008 to 2020.

# METHODS

## Participating hospitals

Through October 2020 to October 2021, active surveillance for CDI was conducted for three months at tertiary and general hospitals in Korea. The number of participating hospitals in each region was determined based on the population size of the region (**Fig. 1**). The participating hospitals had infectious disease specialists serving as investigators along with a laboratory system for diagnosing CDI.

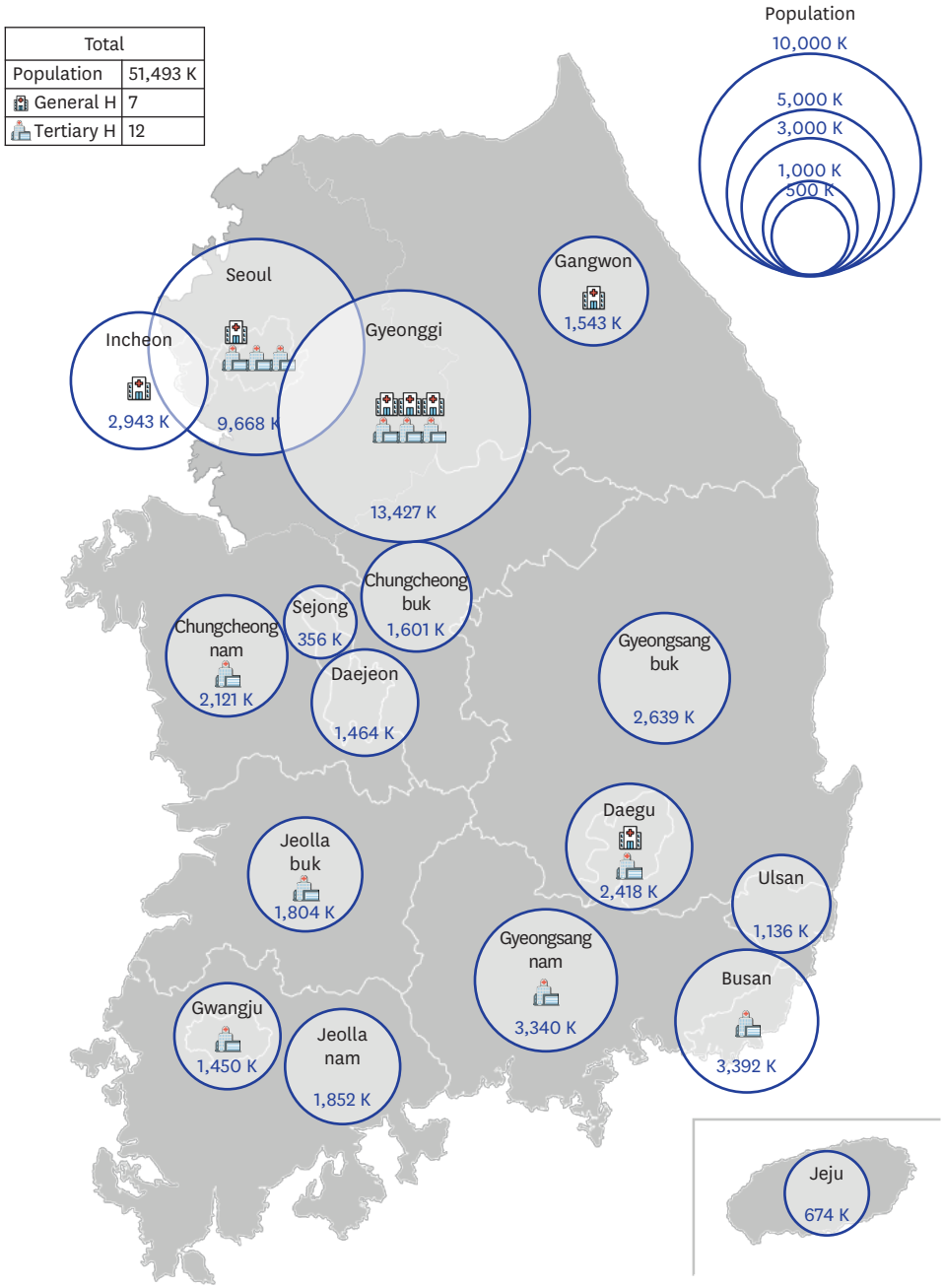


**Fig. 1.** Geographic information of the participating hospitals. The size of the circle represents the population of each administrative district in 2020 by Korean Statistical Information Service.


https://doi.org/10.3346/jkms.2024.39.e118

### Active surveillance program for diarrhoea and diagnosis of CDI

During the study period, investigators monitored all admitted patients to select those who had newly developed unformed stools, three or more times per day, by using an electronic surveillance program for diarrhoea or reviewing electronic medical records (EMRs). Patients with unexplained diarrhoea were tested for CDI. If CDI tests were not performed in patients with diarrhoea, the researchers would leave a note to the physicians in charge to perform the CDI test.

### Definition

To diagnose CDI, glutamate dehydrogenase (GDH), nucleic acid amplification test (NAAT), or enzyme immunoassay (EIA) toxin A&B assays were performed according to the hospital property. CDI was confirmed when an infectious disease physician suspected CDI based on clinical characteristics, and the EIA toxin A&B assay or NAAT was positive. These diagnostic criteria were determined with some modifications from the Society for Healthcare Epidemiology of America/Infectious Diseases Society of America (SHEA/IDSA) guidelines.[13]

The incidence of CDI was estimated based on the number of CDI cases per 10,000 patient-days or per 1,000 admissions. All CDI cases were included in the incidence rate regardless of recurrence. Patients diagnosed with CDI who developed diarrhoea at least 72 hours after admission or within 2 months of the last discharge were considered to have healthcare-associated CDI (HA-CDI). Patients with CDI who did not meet the criteria for HA-CDI were considered community-acquired CDI (CA-CDI).[14] The researchers investigated the medical history through medical records and interviews.

### Incidence of CDI from the national data of the HIRA

We obtained big data from the HIRA from 2008 to 2020 with permission (M20211021591). All admitted patients aged ≥ 20 years who were diagnosed with A047 as the main or sub-diagnosis were included. According to the Korean Standard Classification of Diseases, A047 includes enteritis caused by *C. difficile* and pseudomembranous colitis. Patients who were admitted for 0 days and those with admission costs for 0 days were excluded from the study. As for the incidence rate per population, data from Statistics Korea were used as the denominator because the National Health Insurance System of Korea covers almost the entire population.[15]

### Statistical analysis

Continuous variables were analysed using the Mann–Whitney *U* test to determine differences. The incidence trend was analysed using a linear regression model. Statistical analyses were performed using SPSS version 27 (IBM Corp., Armonk, NY, USA).

### Ethics statement

This study was conducted in accordance with the guidelines of the Declaration of Helsinki. The study protocols were reviewed and approved by the Institutional Review Board of Hanyang University Hospital and written informed consent was obtained from all the participants (approval no. HYUH 2020-06-046 for active surveillance; HYUH 2021-02-019 for big data). All methods were performed in accordance with relevant guidelines and regulations.

# RESULTS

## Prospective observational study with active surveillance

### *Characteristics of the participating hospitals*

Initially, 12 tertiary hospitals and seven general hospitals participated in this study (**Fig. 1**). A tertiary hospital is a teaching hospital affiliated with a medical school that provides a higher level of medical services and expertise than general hospitals. During the study period, one tertiary hospital was temporarily converted into a coronavirus disease 2019 specialized hospital, which made the demographic characteristics of the admitted patients different from those of other hospitals. This hospital was therefore excluded. Finally, 11 tertiary hospitals and seven general hospitals, were included. The characteristics of the participating hospitals are listed in **Table 1**.

Of these, 13 hospitals screened patients with diarrhoea using an electronic surveillance program for diarrhoea, and 5 hospitals manually reviewed the EMR for the detection of patients with diarrhoea. Among 18 hospitals, nine (50%) hospitals performed GDH, 15 (83.3%) hospitals performed polymerase chain reaction as NAAT, 18 (100%) hospitals performed EIA toxin A&B assay, and nine (50%) hospitals performed *C. difficile* culture tests.

### *Incidence of CDI*

Within 1,288,571 patient-days and 193,264 admissions, 30,212 patients had diarrhoea and 907 patients were diagnosed with CDI. Therefore, the incidence was 7.04 per 10,000 patient-days and 4.69 per 1,000 admissions.

In the tertiary hospitals, 24,592 patients complained of diarrhoea. Among them, 646 patients (2.6%) were confirmed as having CDI. Total CDI/10,000 patient-days was 6.38 (range: 3.25–12.05) and total CDI/1,000 admissions was 4.18 (range: 1.92–8.59). **Table 2** shows the incidence of CDI at each tertiary hospital. Among patients with CDI, a total of 39 (6%) complained of diarrhoea less than 72 hours after the admission. Therefore, the HA-CDI incidence rate in tertiary hospitals was 5.99 per 10,000 patient-days and 3.93 per 1,000 admissions.

In the general hospitals, 5,620 patients complained of diarrhoea. Among these, 261 patients (4.6%) were confirmed as having CDI. Total CDI/10,000 patient-days was 9.45 (range: 5.68–13.90) and CDI/1,000 admissions was 6.73 (range: 3.18–15.85). **Table 2** shows the incidence of CDI at each hospital. Among patients with CDI, 29 (11.1%) complained of diarrhoea within 72 hours after the admission. Therefore, the HA-CDI incidence rate in general hospitals was 8.4 per 10,000 patient-days and 5.98 per 1,000 admissions. Therefore, as for the origin

**Table 1.** Characteristics of participating hospitals

| Variables | A | B | C | E | F | G | H | I | J | L | M | N | O | P | Q | R | S | T |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Hospital type | T | T | T | T | T | T | T | T | T | G | T | G | G | G | G | G | G | T |
| Screening method | E | M | E | M | E | E | M | M | E | E | E | E | E | E | M | E | E | E |
| Capacity of hospital | 855 | 895 | 1,205 | 684 | 799 | 894 | 1,371 | 1,084 | 1,334 | 725 | 700 | 670 | 613 | 463 | 315 | 648 | 402 | 762 |
| Laboratory test for CDI | | | | | | | | | | | | | | | | | | |
| GDH | O | | O | | | O | | O | O | O | | | O | O | | | O | |
| PCR | O | O | O | O | O | | O | O | | O | O | O | O | O | O | O | O | O |
| EIA toxin A&B | O | O | O | O | O | O | O | O | O | O | O | O | O | O | O | O | O | O |
| Culture | O | | | O | O | | | O | O | | O | | O | O | | O | | |

T = tertiary hospital, G = general hospital, E = electronic surveillance program, M = manual review of electronic medical records, CDI = *Clostridioides difficile* infection, GDH = glutamate dehydrogenase, PCR = polymerase chain reaction, EIA = enzyme immunoassay, O = Tests performed at the hospital.


https://doi.org/10.3346/jkms.2024.39.e118

JKMS

**Table 2.** CDI incidence rates in participating hospitals

| Variables | Tertiary hospitals | | | | | | | | | | | General hospitals | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | A | B | C | E | F | G | H | I | J | M | T | L | N | O | P | Q | R | S |
| No. of diarrheal patients | 7,267 | 866 | 353 | 2,726 | 651 | 4,135 | 2,434 | 897 | 758 | 3,510 | 995 | 239 | 1,337 | 1,344 | 935 | 309 | 1,164 | 292 |
| No. of CDI patients | 151 | 26 | 56 | 28 | 44 | 39 | 54 | 85 | 57 | 65 | 41 | 53 | 37 | 43 | 21 | 29 | 48 | 30 |
| No. of healthcare-associated CDI patients | 136 | 25 | 56 | 26 | 44 | 36 | 50 | 80 | 57 | 60 | 37 | 53 | 30 | 38 | 17 | 24 | 47 | 23 |
| No. of community-associated CDI patients | 15 | 1 | 0 | 2 | 0 | 3 | 4 | 5 | 0 | 5 | 4 | 0 | 7 | 5 | 4 | 5 | 1 | 7 |
| Patient-days | 131,824 | 80,113 | 121,422 | 66,131 | 75,565 | 67,555 | 94,363 | 119,642 | 139,856 | 53,920 | 62,122 | 55,152 | 47,851 | 44,294 | 36,979 | 20,866 | 40,252 | 30,664 |
| Admission | 17,586 | 13,559 | 17,227 | 10,701 | 12,441 | 10,753 | 11,404 | 14,077 | 26,625 | 10,199 | 9,896 | 4,419 | 7,290 | 7,255 | 6,613 | 1,830 | 6,046 | 5,343 |
| CDI/Patient-days*$10^4$ | 11.45 | 3.25 | 4.61 | 4.23 | 5.82 | 5.77 | 5.72 | 7.10 | 4.08 | 12.05 | 6.60 | 9.61 | 7.73 | 9.71 | 5.68 | 13.90 | 11.92 | 9.78 |
| HA-CDI/Patient-days*$10^4$ | 10.32 | 3.12 | 4.61 | 3.93 | 5.82 | 5.33 | 5.30 | 6.69 | 4.08 | 11.13 | 5.96 | 9.61 | 6.27 | 8.58 | 4.60 | 11.50 | 11.68 | 7.50 |
| CDI/admission*$10^3$ | 8.59 | 1.92 | 3.25 | 2.62 | 3.54 | 3.63 | 4.74 | 6.04 | 2.14 | 6.37 | 4.14 | 11.99 | 5.08 | 5.93 | 3.18 | 15.85 | 7.94 | 5.62 |
| HA-CDI/admission*$10^3$ | 7.73 | 1.84 | 3.25 | 2.43 | 3.54 | 3.35 | 4.38 | 5.68 | 2.14 | 5.88 | 3.74 | 11.99 | 4.12 | 5.24 | 2.57 | 13.11 | 7.77 | 4.30 |
| No. of 1st episode of CDI | 137 | 25 | 54 | 26 | 42 | 37 | 52 | 81 | 54 | 59 | 34 | 49 | 36 | 43 | 19 | 26 | 42 | 28 |

CDI = *Clostridioides difficile* infection, HA-CDI = healthcare-associated CDI.

of CDI, most were HA-CDI (92.5%), and CA-CDI represented a low proportion (7.5%): 6.03% in tertiary hospitals and 11.1% in general hospitals (**Table 2**).

Comparing the CDI incidences between the hospitals with electronic surveillance programs for diarrhoea and those using manual screening of EMR, the incidence rates of CDI in the former hospitals tended to be higher than those in the latter hospitals, but without statistical significance. The median CDI incidence rate was 5.72 per 10,000 patient-days and 4.74 per 1,000 admissions by the manual screening method and 7.73 per 10,000 patient-days and 5.08 per 1,000 admissions by the electronic screening method ($P = 0.349$ and $P = 0.73$, respectively, by the Mann-Whitney $U$ test).

### Incidence of CDI from the national data of the HIRA from 2008 to 2020

Using national data from the HIRA, the annual incidences of CDI between 2008 and 2020 were measured and compared. The incidence of CDI was assessed per 10,000 patient days, 1,000 admissions, and 100,000 individuals. From 2008 to 2020, the incidence of CDI gradually increased significantly. Based on the CDI incidence per 10,000 patient-days, the incidence increased from 1 to 5.1 in tertiary hospitals ($P < 0.001$, adjusted $R^2 = 0.955$), and from 0.6 to 5 in general hospitals ($P < 0.001$, adjusted $R^2 = 0.971$) (**Fig. 2**). Based on the CDI incidence per 1,000 admissions, the incidence increased from 0.8 to 2.8 in tertiary hospitals ($P < 0.001$, adjusted $R^2 = 0.949$) and from 0.5 to 3.2 in general hospitals ($P < 0.001$, adjusted $R^2 = 0.963$). The CDI incidence per 100,000 individuals also increased significantly from 6.9 to 56.9 in all hospital types ($P < 0.001$, adjusted $R^2 = 0.985$). The gross incidence rate of CDI increased approximately 3-fold in tertiary hospitals, general hospitals, and all hospitals in Korea over a period of 10 years from 2011 (**Fig. 2**).

When comparing the incidence rate of CDI between prospective active surveillance and retrospective national data analysis, the incidence rate was underestimated in the national data analysis, particularly in general hospitals.

## DISCUSSION

In this study, a prospective multicentre observational study using an active surveillance program, and an analysis of the data from the HIRA, we demonstrated that the incidence of CDI in Korea was as high as that in the U.S. and other European countries. This is in contrast to previously published studies where the value was found to be lower than that in Western countries and similar to that in other Asian countries.[3,16,17]

Furthermore, the incidence of CDI in Korea has gradually increased over the past 13 years. In a previous prospective study conducted in 2009 at a single centre in Korea, the incidence rate of CDI was 7.16 cases per 10,000 patients-day,[9] and the value in the same hospital increased to 11.45 cases per 10,000 patients-days in 2020–2021 in this study. There may be several reasons for the increase in CDI incidence: First, the older adult population has been increasing, and broad-spectrum antibiotics have been used more widely in Korea.[11,12] Second, physicians recognised CDI considerably more than they did a decade ago, and tested for CDI more frequently.


https://doi.org/10.3346/jkms.2024.39.e118

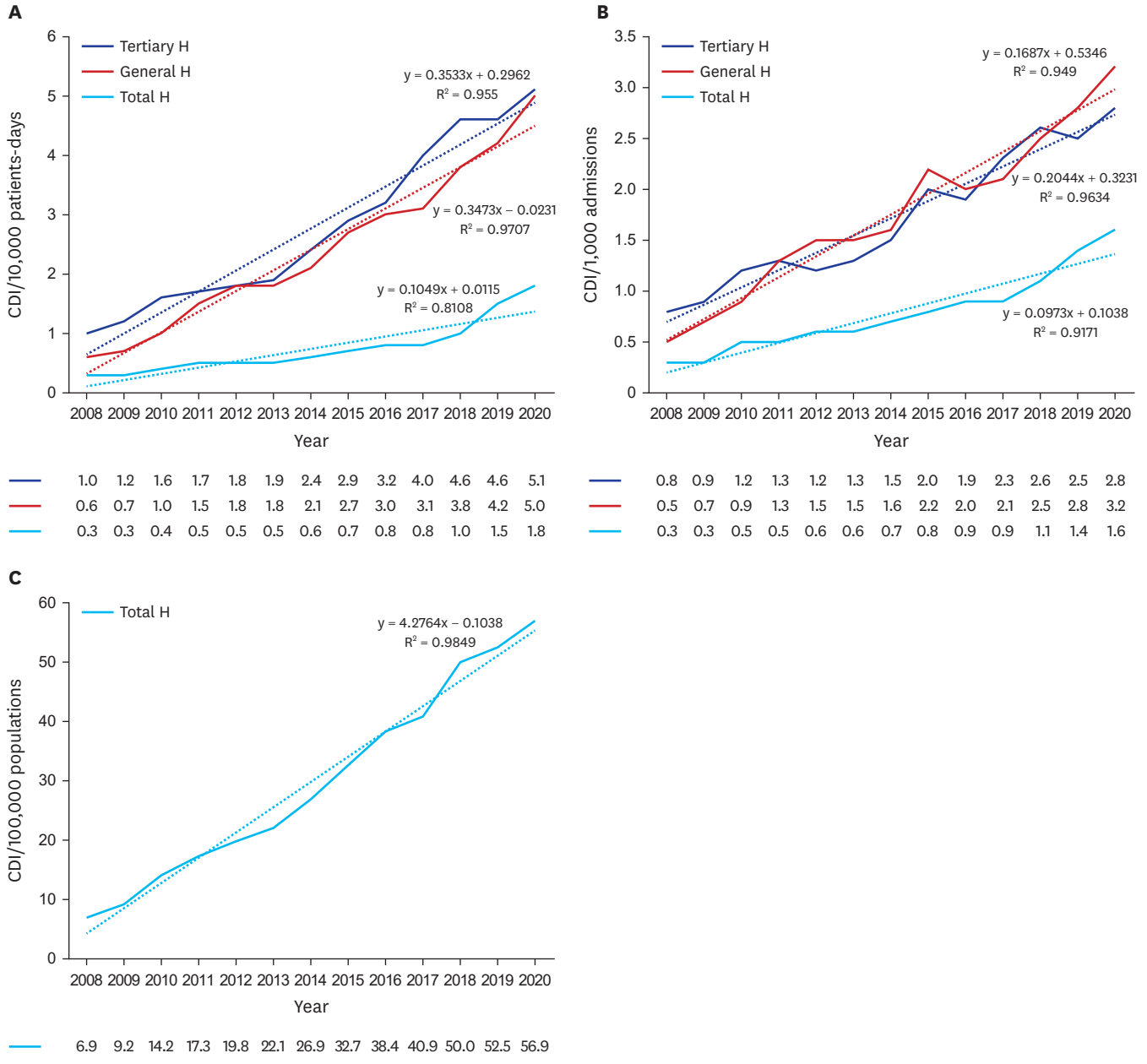


**Fig. 2.** CDI incidence according to hospital type in Korea using data from the Health Insurance Review & Assessment Service (HIRA) from 2008 to 2020: (**A**) per 10,000 patient-days, (**B**) per 1,000 admissions, (**C**) per 100,000 population years.
CDI = *Clostridioides difficile* infection.

Third, the diagnostic method has changed; the EIA toxin A&B assay has been the most common diagnostic tool for CDI in Korea, and the NAAT or GDH tests have been introduced and covered by insurance since 2017 in Korea[18]; however, the CDI incidence might be overestimated because of the high detection rate of NAAT.[19]

According to the SHEA/IDSA guidelines, a suitable stool sample could be diagnosed as CDI by NAAT alone or by the stool toxin test as part of a multiple step algorithm.[13] We applied these guidelines to diagnose CDI when NAAT was positive, or when GDH and toxins were positive. However, the GDH test was performed in only 50% of participating hospitals,


https://doi.org/10.3346/jkms.2024.39.e118

making it difficult to recommend as a diagnostic standard. Therefore, only toxin test results without GDH were included in the diagnostic criteria, in this study. Confirming the diagnosis of CDI using a single test is challenging. The key to diagnosing CDI is to suspect it in patients experiencing unformed stools three or more times per day without a clear cause, ordering the necessary diagnostic tests for the diagnosis of CDI, and performing the tests appropriately under anaerobic conditions.

While we collected the CDI cases among hospitalised patients, 6.03% and 11.1% of patients with CDI in tertiary and general hospitals, respectively, were defined as CA-CDI. The proportion of CA-CDI in this study was lower than that reported in the U.S. or Europe[17,20,21] and we considered that the proportion of CA-CDI in our study was underestimated. Since we enrolled patients with diarrhoea among hospitalised patients who were not in outpatient clinics or emergency rooms, patients with CA-CDI who were not hospitalised may have been missed in this study. Additionally, the participating hospitals were general or tertiary hospitals, and patients with mild CA-CDI may have visited primary outpatient clinics. Therefore, to determine the approximate incidence of CA-CDI in Korea, a prospective study including outpatient clinics and emergency units is necessary.

The incidence rate of CDI in hospitals is dependent on the appropriate detection of patients with diarrhoea as well as using appropriate tests for CDI. As expected, the incidence rates of active surveillance were higher than those of the HIRA, especially in general hospitals. To detect patients with diarrhoea without fail, a hospital in the U.S. reported the adoption of a policy allowing nurses to independently order stool samples for new patients with CDI symptoms.[22] In this study, 64% of tertiary hospitals and 86% of general hospitals employed electronic surveillance programs to detect patients with diarrhoea, which successfully reduced the workload of the researchers. The programs for surveying diarrhoea were easily created in each hospital using an EMR system. The incidence of CDI tended to be higher in hospitals with electronic surveillance programs for diarrhoea; however, this difference was not statistically significant. Even with this screening system in place, screening all relevant patients is difficult, which might partly explain the difference in incidence rates among hospitals.

According to the Korea National Antimicrobial Use Analysis System data for 2021, antibiotic usage in general hospitals is higher than that in tertiary hospitals. Indeed, the incidence rate of CDI in the general hospitals, participating in the study, was higher than that in the tertiary hospitals. However, national data have shown that the CDI incidence rate in secondary hospitals is lower than that in tertiary hospitals. The lack of awareness of CDI among medical staff, poor detection of relevant patients with diarrhoea, and lack of available CDI tests might contribute to the low incidence rate in general hospitals.

Hospitalisation is an important risk factor for the acquisition of CDI. As the CDI incidence rate and average length of stay (ALS)[23] in each hospital showed two- to three-fold differences among the participating hospitals, we analysed the association between the turnover rate of beds (TRB)[24] or ALS and CDI incidence rates in the participating hospitals. The incidence rate of CDI was negatively correlated with TRB and positively correlated with ALS (data not shown). However, the incidence of CDI in hospitals is influenced by many factors, including antibiotic usage and hospital infection control (environmental cleaning and isolation of patients with CDI). Therefore, surveying multiple risk factors for CDI in hospitals is necessary to determine the relationship between the incidence rate of CDI and TRB or ALS.


https://doi.org/10.3346/jkms.2024.39.e118

Despite the overall increase in CDI worldwide, England and the United States have recently shown a decrease in the incidence of HA-CDI.[25,26] Particularly in England, there has been an approximately 80% decrease in incidence since 2006. The most probable reason for this decline is the restriction of fluoroquinolone and cephalosporin use, which showed a high correlation with CDI occurrence. Additionally, *C. difficile* is a spore-forming bacterium that exhibits resistance to alcohol and can survive for long periods in the environment, making it a potential reservoir for persistent infections and reinfection.[10] Therefore, infection control is important for decreasing the risk of *C. difficile* transmission in hospitals.[27] In Korea, the predominant form of CDI is largely associated with HA-CDI. For the correct management of CDI, reinforced antibiotic stewardship and multidisciplinary infection control measures are necessary.

In conclusion, the incidence of CDI in Korea increased from 2008 to 2020, and its recent value was as high as that in the U.S. and Europe. CDI is underestimated, particularly in general hospitals in Korea.

## REFERENCES

1. Martin JS, Monaghan TM, Wilcox MH. *Clostridium difficile* infection: epidemiology, diagnosis and understanding transmission. *Nat Rev Gastroenterol Hepatol* 2016;13(4):206-16. PUBMED | CROSSREF
2. Tschudin-Sutter S, Kuijper EJ, Durovic A, Vehreschild MJ, Barbut F, Eckert C, et al. Guidance document for prevention of *Clostridium difficile* infection in acute healthcare settings. *Clin Microbiol Infect* 2018;24(10):1051-4. PUBMED | CROSSREF
3. Ho J, Wong SH, Doddangoudar VC, Boost MV, Tse G, Ip M. Regional differences in temporal incidence of *Clostridium difficile* infection: a systematic review and meta-analysis. *Am J Infect Control* 2020;48(1):89-94. PUBMED | CROSSREF
4. Marra AR, Perencevich EN, Nelson RE, Samore M, Khader K, Chiang HY, et al. Incidence and outcomes associated with *Clostridium difficile* infections: a systematic review and meta-analysis. *JAMA Netw Open* 2020;3(1):e1917597. PUBMED | CROSSREF
5. Borren NZ, Ghadermarzi S, Hutfless S, Ananthakrishnan AN. The emergence of *Clostridium difficile* infection in Asia: a systematic review and meta-analysis of incidence and impact. *PLoS One* 2017;12(5):e0176797. PUBMED | CROSSREF
6. Collins DA, Sohn KM, Wu Y, Ouchi K, Ishii Y, Elliott B, et al. *Clostridioides difficile* infection in the Asia-Pacific region. *Emerg Microbes Infect* 2019;9(1):42-52. PUBMED | CROSSREF
7. Kim YS, Han DS, Kim YH, Kim WH, Kim JS, Kim HS, et al. Incidence and clinical features of *Clostridium difficile* infection in Korea: a nationwide study. *Epidemiol Infect* 2013;141(1):189-94. PUBMED | CROSSREF
8. Han SH, Kim H, Lee K, Jeong SJ, Park KH, Song JY, et al. Epidemiology and clinical features of toxigenic culture-confirmed hospital-onset Clostridium difficile infection: a multicentre prospective study in tertiary hospitals of South Korea. *J Med Microbiol* 2014;63(Pt 11):1542-51. PUBMED | CROSSREF
9. Kim J, Pai H, Seo MR, Kang JO. Epidemiology and clinical characteristics of *Clostridium difficile* infection in a Korean tertiary hospital. *J Korean Med Sci* 2011;26(10):1258-64. PUBMED | CROSSREF
10. Czepiel J, Dróżdż M, Pituch H, Kuijper EJ, Perucki W, Mielimonka A, et al. *Clostridium difficile* infection: review. *Eur J Clin Microbiol Infect Dis* 2019;38(7):1211-21. PUBMED | CROSSREF
11. Kim Y, Chae J, Shin S, Jo G, Shin J, Kim B, et al. Trends in national pharmaceutical expenditure in Korea during 2011–2020. *Infect Chemother* 2023;55(2):237-46. PUBMED | CROSSREF
12. Baek JY, Lee E, Jung HW, Jang IY. Geriatrics fact sheet in Korea 2021. *Ann Geriatr Med Res* 2021;25(2):65-71. PUBMED | CROSSREF
13. McDonald LC, Gerding DN, Johnson S, Bakken JS, Carroll KC, Coffin SE, et al. Clinical practice guidelines for *Clostridium difficile* infection in adults and children: 2017 update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). *Clin Infect Dis* 2018;66(7):e1-48. PUBMED | CROSSREF
14. Dubberke ER, Carling P, Carrico R, Donskey CJ, Loo VG, McDonald LC, et al. Strategies to prevent *Clostridium difficile* infections in acute care hospitals: 2014 update. *Infect Control Hosp Epidemiol* 2014;35(6):628-45. PUBMED | CROSSREF

15. Kim JA, Yoon S, Kim LY, Kim DS. Towards actualizing the value potential of Korea Health Insurance Review and Assessment (HIRA) data as a resource for health research: strengths, limitations, applications, and strategies for optimal use of HIRA data. *J Korean Med Sci* 2017;32(5):718-28. PUBMED | CROSSREF
16. Choi HY, Park SY, Kim YA, Yoon TY, Choi JM, Choe BK, et al. The epidemiology and economic burden of *Clostridium difficile* infection in Korea. *BioMed Res Int* 2015;2015:510386. PUBMED | CROSSREF
17. Finn E, Andersson FL, Madin-Warburton M. Burden of *Clostridioides difficile* infection (CDI) - a systematic review of the epidemiology of primary and recurrent CDI. *BMC Infect Dis* 2021;21(1):456. PUBMED | CROSSREF
18. Chung HS, Park JS, Shin BM, Yoo HM, Kim H, Cho J, et al. Nationwide survey for current status of laboratory diagnosis of *Clostridioides difficile* infection in Korea. *J Korean Med Sci* 2022;37(5):e38. PUBMED | CROSSREF
19. Gould CV, Edwards JR, Cohen J, Bamberg WM, Clark LA, Farley MM, et al. Effect of nucleic acid amplification testing on population-based incidence rates of *Clostridium difficile* infection. *Clin Infect Dis* 2013;57(9):1304-7. PUBMED | CROSSREF
20. Kutty PK, Woods CW, Sena AC, Benoit SR, Naggie S, Frederick J, et al. Risk factors for and estimated incidence of community-associated *Clostridium difficile* infection, North Carolina, USA. *Emerg Infect Dis* 2010;16(2):197-204. PUBMED | CROSSREF
21. Khanna S, Pardi DS, Aronson SL, Kammer PP, Orenstein R, St Sauver JL, et al. The epidemiology of community-acquired *Clostridium difficile* infection: a population-based study. *Am J Gastroenterol* 2012;107(1):89-95. PUBMED | CROSSREF
22. Bartlett A, Montgomery A, Hammer K, Singhal S, Lo TS. Does clinician-initiated Clostridioides difficile testing improve outcomes of patients with *Clostridioides difficile* infection? *Am J Infect Control* 2023;51(10):1085-8. PUBMED | CROSSREF
23. OECD. *Health at a Glance 2021*. Paris, France: OECD; 2021.
24. Aloh HE, Onwujekwe OE, Aloh OG, Nweke CJ. Is bed turnover rate a good metric for hospital scale efficiency? A measure of resource utilization rate for hospitals in Southeast Nigeria. *Cost Eff Resour Alloc* 2020;18(1):21. PUBMED | CROSSREF
25. Dingle KE, Didelot X, Quan TP, Eyre DW, Stoesser N, Golubchik T, et al. Effects of control interventions on Clostridium difficile infection in England: an observational study. *Lancet Infect Dis* 2017;17(4):411-21. PUBMED | CROSSREF
26. Guh AY, Mu Y, Winston LG, Johnston H, Olson D, Farley MM, et al. Trends in U.S. burden of *Clostridioides difficile* infection and outcomes. *N Engl J Med* 2020;382(14):1320-30. PUBMED | CROSSREF
27. Barker AK, Ngam C, Musuuza JS, Vaughn VM, Safdar N. Reducing *Clostridium difficile* in the inpatient setting: a systematic review of the adherence to and effectiveness of *C. difficile* prevention bundles. *Infect Control Hosp Epidemiol* 2017;38(6):639-50. PUBMED | CROSSREF