



Epidemiological Features of Healthcare-associated *Acinetobacter baumannii* Infections in Taiwan during 2008 – 2019

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Background: *Acinetobacter baumannii* can reside in humans without causing infection or symptoms but can opportunistically cause community and nosocomial infections. Few studies from Taiwan have used national-level data to investigate antibiotic resistance rates of *A. baumannii* infections in the intensive care units (ICUs) of medical centers. **Aim:** This study determined the number of infection sites of *A. baumannii* and the resistance rates of carbapenem-resistant *A. baumannii* (CRAB) infections in ICUs in Taiwan, and identified trends over time, variations of infection site, and factors associated with resistance. **Methods:** This study used the database provided by Taiwan's Centers for Disease Control. Yearly, Taiwan Nosocomial Infections Surveillance System Surveys from 2008 to 2019 were analyzed, including data on the site of infection and resistance rates of *A. baumannii* and patient and hospital characteristics. **Results:** On average, 21 hospitals as medical center/year participated in the survey, and 6803 *A. baumannii* isolates were identified. All isolates were health care-related infections. The most frequent sites of infection were the urinary tract (50.6%), respiratory tract (19.6%), bloodstream (18.2%), surgical wounds (4.3%), and others (7.4%). Infection rates were the highest in the urinary tract in 2019 (63.6%; $P < 0.001$). On average, the rate of carbapenem resistance was 66.6% (95% confidence interval: 63.1–70.1) among ICU patients at medical centers. Considerable regional differences were observed, with the highest rates of resistance in the central regions. Higher resistance rates were observed between 2019 and 2020 COVID-19 pandemic (74.2%). **Conclusion:** This is the first report on the prevalence of health care-related *A. baumannii* infection in Taiwan in 2008–2019. Several invasive diseases, such as urinary tract infections, are associated with higher rates of carbapenem resistance. The resistance rate of CRAB in Taiwan is exceptionally high. The current big-data-derived findings may inform future surveillance and research efforts in Taiwan.

Key words: *Acinetobacter baumannii*, carbapenem, healthcare-associated infections

INTRODUCTION

Over 65 *Acinetobacter* species have been identified using molecular approaches.¹ *Acinetobacter* are Gram-negative, strictly aerobic, nonfermentative, oxidase-negative, catalase-positive, and nonpigmented or pale yellow-to gray-pigmented bacteria.² *Acinetobacter calcoaceticus*–*baumannii* complex (ACBC) includes closely

related species displaying similar phenotypic and biochemical properties, including *A. calcoaceticus*, *A. baumannii*, *Acinetobacter pittii*, *Acinetobacter nosocomialis*, *Acinetobacter seifertii*, and *Acinetobacter dijkshoorniae*, and molecular methods are required to identify them.³ *Acinetobacter* can live for long periods on surfaces and equipment if these surfaces

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are not properly cleaned. The germs can spread between people through contact with these contaminated surfaces or equipment, or through person to person spread, often through contaminated hands.⁴ All the aforementioned *Acinetobacter* species other than *A. calcoaceticus* are associated with human diseases, with *A. baumannii* being the most common worldwide.⁵ *Acinetobacter* can reside in humans without causing infection or symptoms but can opportunistically cause community and nosocomial infections, predominantly ventilator-associated pneumonia and bloodstream, wound, urinary tract, and skin and soft-tissue infections, especially among critically ill patients in intensive care units (ICUs).⁶ Typical symptoms of pneumonia include fever, chills, and cough. The symptoms of bloodstream infection might include fever, chills, vomiting, and confusion. A wound infection might cause fever and redness, increasing pain, and pus around the wound. The symptoms of urinary tract infection include frequent urination, pain or burning during urination, blood in the urine, cloudy or foul-smelling urine, and altered mental status. In severely ill patients, *Acinetobacter* infection may lead to death.⁷

Unfortunately, a considerable increase in the cases of multidrug-resistant (MDR) *A. baumannii* isolates has been reported.⁸ Apart from innate resistance to several antibiotics, *A. baumannii* genomic plasticity is suited for acquiring or upregulating resistance genes, thereby curtailing effective therapeutic options and increasing mortality rates.⁹ *A. baumannii* also has several potential virulence traits that allow it to persist in the environment, adhere to biotic surfaces, invade host cells, and evade the human host immune system.¹⁰

Few studies from Taiwan have used national-level data to investigate antibiotic resistance rates of *A. baumannii* infections in the ICUs of medical centers. Therefore, this study examined the infection sites and antibiotic resistance rates of *A. baumannii* infection in Taiwan between 2008 and 2019.

MATERIALS AND METHODS

Ethical policy

This study was approved by the Research Ethics Committee of National Taiwan University (IRB No. 202109EM011).

Data source

This study employed Taiwan's Centers for Disease Control (CDC) public network database - the Annual Statistics of Communicable Diseases and Surveillance Report (ASCDSR) - for the years 2008–2019,¹¹ which included all notifiable communicable diseases in categories 1–5 specified by the Communicable Disease Control Act. These data are provided to maintain information on Taiwan's diseases

transparent and current. To ensure information security and prevent personal information leaks, the ASCDSR (including Taiwan Nosocomial Infections Surveillance System data) does not store personal information and stores only secondary statistics. These statistics enable the public, researchers, and the press to access current information on health care-associated infection (HAI) surveillance data in Taiwan at any time.

The present study collected the data on the date when confirmed cases of health care-associated *A. baumannii* infection were reported to Taiwan's health department. The database does not contain patients' medical histories or signs and symptoms.

Data analysis and statistics

This was a retrospective historical study on all health care-associated *A. baumannii* infections in ICUs at medical centers in Taiwan between 2008 and 2019. Types of ICUs include medical ICUs, surgical ICUs, cardiology ICUs, pediatric ICUs, and medical/surgical ICUs. On the basis of the ASCDSR, the number of confirmed cases of health care-associated *A. baumannii* infection from January 2008 to December 2019 were determined, and the distribution, differences, and results of epidemiological characteristics (i.e., number of *A. baumannii* strains, infection sites, number of cases, and *A. baumannii* resistance rate) were consolidated.

Descriptive data are expressed as means and summary statistics. The categorical variables were compared using the Chi-square tests, which were performed using SPSS (IBM SPSS Statistics v21; Asia Analytics Taiwan Ltd., Taipei, Taiwan). Chi-square tests were two-sided, with an α level of 0.05. $P < 0.05$ was considered statistically significant.

RESULTS

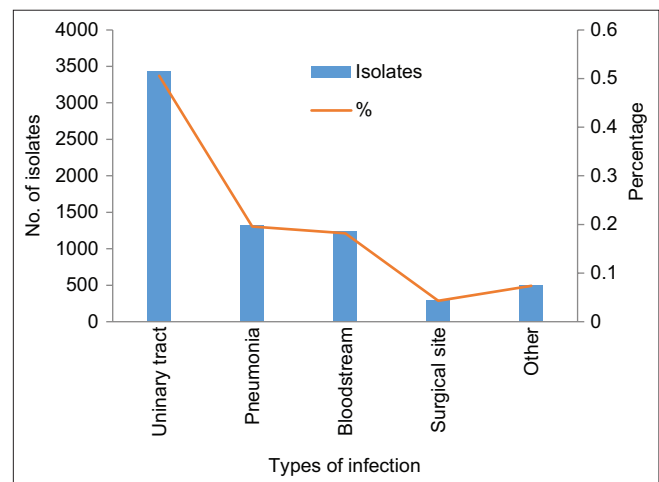
Between 2008 and 2019, the annual distribution of *A. baumannii* strains isolated from the selected infection sites had a statistically significant difference [$P < 0.001$, Table 1].

Among ICU patients with infection from various Taiwanese medical centers during the study period, 3439 isolates (50.55%) of *A. baumannii* were obtained from the urinary tract, 1330 (19.55%) from the respiratory tract, 1237 (18.18%) from the bloodstream, 293 (4.31%) from surgical wounds, and 504 (7.41%) from other sites [Figure 1].

From 2008 to 2019, the total annual number of *A. baumannii* isolates obtained was 648, 795, 843, 835, 799, 581, 444, 459, 397, 329, 343, and 330, respectively. Considering 2-year data (i.e., 2008–2009, 2010–2011, 2012–2013, 2014–2015, 2016–2017, and 2018–2019), 579, 769, 748, 471, 447, and 425 *A. baumannii* isolates, respectively, were obtained from all infection sites; 319, 388, 259, 181, 90, and 93, respectively,

A. baumannii caused HAIsTable 1: Infection site of *Acinetobacter baumannii* isolates from the intensive care units of medical centers, Taiwan, 2008-2019

Variables	Year													P
	2008, n (%)	2009, n (%)	2010, n (%)	2011, n (%)	2012, n (%)	2013, n (%)	2014, n (%)	2015, n (%)	2016, n (%)	2017, n (%)	2018, n (%)	2019, n (%)		
Urinary tract	240 (37.0)	339 (42.6)	364 (43.2)	405 (48.5)	440 (55.1)	308 (53.0)	218 (49.1)	253 (55.1)	246 (62.0)	201 (61.1)	215 (62.7)	210 (63.6)	<0.001	
Pneumonia	169 (26.1)	150 (18.9)	212 (25.1)	176 (21.1)	146 (18.3)	113 (19.4)	106 (23.9)	75 (16.3)	51 (12.8)	39 (11.9)	54 (15.7)	39 (11.8)		
Bloodstream	146 (22.5)	205 (25.8)	146 (17.3)	158 (18.9)	130 (16.3)	100 (17.2)	75 (16.9)	82 (17.9)	62 (15.6)	53 (16.1)	37 (10.8)	43 (13.0)		
Surgical site	41 (6.3)	28 (3.5)	43 (5.1)	37 (4.4)	27 (3.4)	29 (5.0)	13 (2.9)	15 (3.3)	16 (4.0)	15 (4.6)	15 (4.4)	14 (4.2)		
Others	52 (8.0)	73 (9.2)	78 (9.3)	59 (7.1)	56 (7.0)	31 (5.3)	32 (7.2)	34 (7.4)	22 (5.5)	21 (6.4)	22 (6.4)	24 (7.3)		

**Figure 1:** Distribution of isolates *Acinetobacter baumannii* by types of infection in the intensive care units of medical centers in Taiwan from 2008 to 2019

from the respiratory tract; 351, 304, 230, 157, 115, and 80, respectively, from the bloodstream; and 69, 80, 56, 28, 31, and 29, respectively, from surgical wounds [Figure 2].

The annual drug resistance testing results of *A. baumannii* in the ICU patients are presented in Figure 3. From 2008 to 2019, 56.3%, 59.7%, 66.8%, 65.2%, 71.2%, 72.9%, 63.7%, 64.3%, 63.6%, 71.5%, 70.2%, and 74.2% of the isolates, respectively, were drug resistant.

DISCUSSION

HAIs increase duration of hospitalization, hospitalization cost, and mortality rate,¹² and infection surveillance play a crucial role in nosocomial infection control. Infection surveillance allows understanding of the occurrence and distribution of nosocomial infection and represents the first step in preventing and controlling HAIs.¹³ In the 1970s, the US CDC and Prevention established the National Nosocomial Infection Surveillance system. The hospitals participating in this system were required to upload their data to the national database, and this marked the initiation of systematic infection surveillance in the United States.¹⁴ This system was consolidated into the National Health-care Safety Network (NHSN) in 2005. The NHSN remains the largest HAI supervision system in the United States. In the 1990s, Taiwanese scholars also proposed that systematic and continuous surveillance and investigation be proactively conducted inside hospitals according to epidemiological methods. Through such initiatives, the infection control personnel can establish long-term trends based on systematic surveillance investigation, and data collected from various time periods can be used for comparison and exploration. This helps

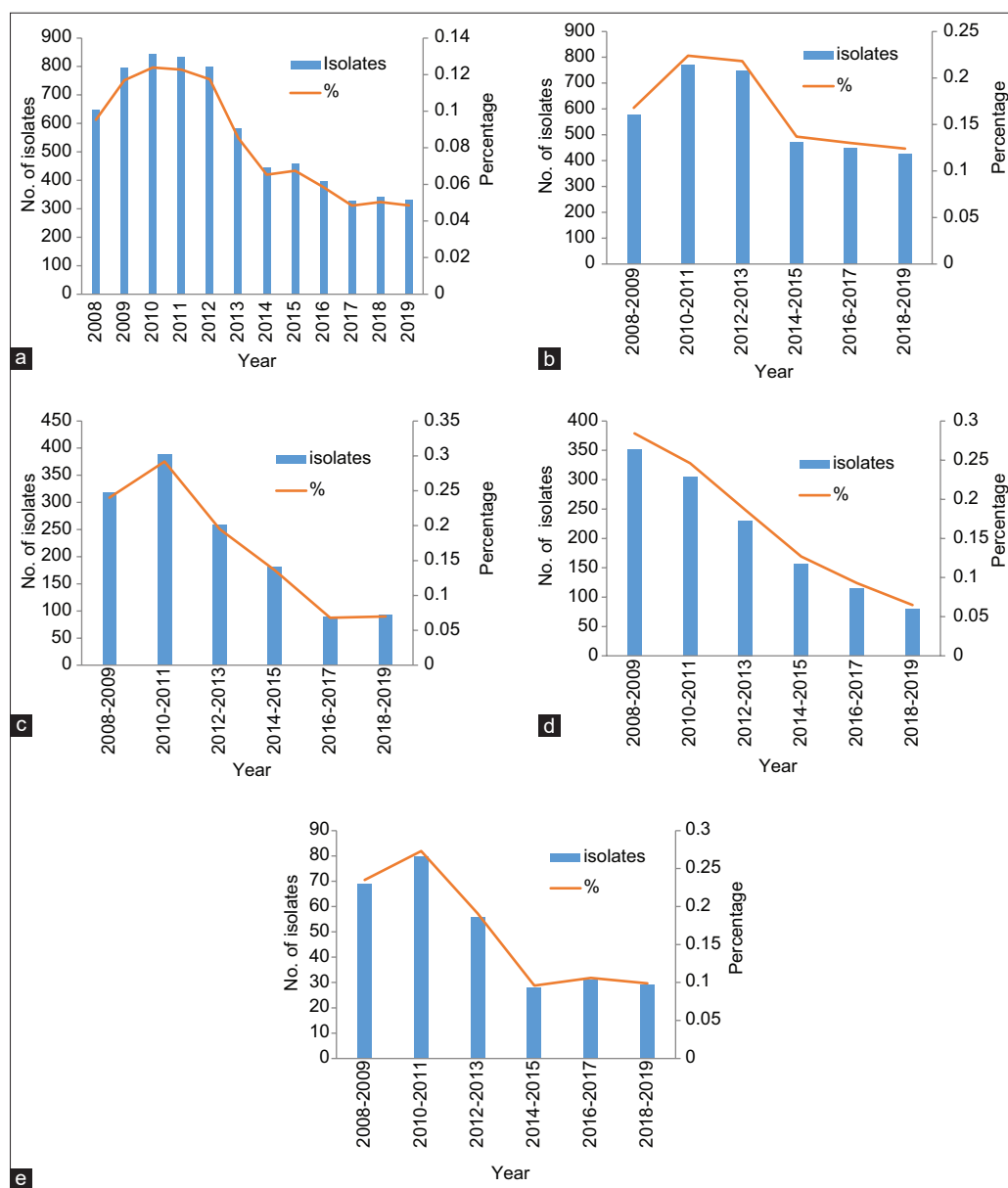


Figure 2: Yearly distribution of *Acinetobacter baumannii* infections associated with infection sites of intensive care units patients from medical centers in Taiwan from 2008 to 2019. (a) all infection sites, (b) urinary tract, (c) respiratory tract, (d) bloodstream, (e) surgical site

in the early detection of changes in the number and density of infection cases. The routine surveillance data and analysis results can be used to draft relevant preventive interventions and evaluate the effectiveness of their implementation.

Each year, approximately 150 million people worldwide develop urinary tract infections.¹⁵ These infections are caused by uropathogenic bacteria, such as MDR *A. baumannii*,¹⁶ which exert considerable medical and social burden because of treatment difficulties and the possibility of recurrence and thus severely reduce patients' quality of life. A related study analyzed *Acinetobacter* isolates identified in the BJC Health

Care System in the period from January 2007 to August 2017.¹⁷ Among 2309 cases of ACBC, 22.2% were isolated from urinary sources; other sources included respirators (33.9%), the soft tissue/musculoskeletal system (31.9%), and the endovascular system (10.4%). Bagińska *et al.*¹⁸ reviewed clinical trials since 1995, including more than 19,000 cases, which considered the anatomical location of ACBC or *A. baumannii* isolates; most isolates originated from the respiratory tract (39.5%) and soft tissue/musculoskeletal system (22.7%). The percentage share of uropathogenic isolates ranged from 6.1% to 29.3%, and the average was 17.1% of all isolates (3410 from 19,957).^{19,20}

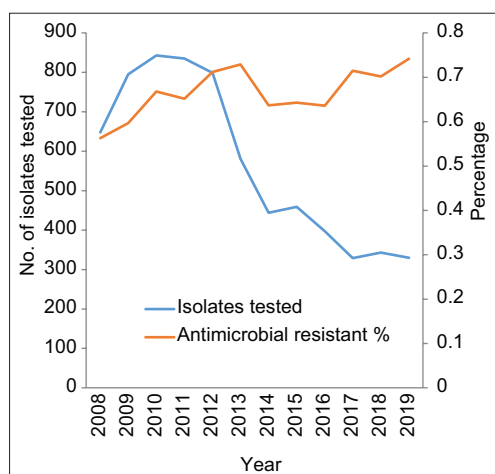
A. baumannii caused HAIs

Figure 3: Antimicrobial resistances of *Acinetobacter baumannii* of healthcare-associated infections in the intensive care units of medical centers in Taiwan from 2008 to 2019

Moreover, an analysis of over 6,803 cases in the present study for the period from 2008 to 2019 indicated that most isolates originated from urinary tract infections (50.6%) and the respiratory tract (19.6%). Taken together, the findings indicate that *A. baumannii* strains constitute a significant percentage of pathogens infecting the urinary tract.

A. baumannii typically exists in abiotic natural environments. Given that it can survive for a long time can easily result in pollution of the hospital environment and can easily develop drug resistance, carbapenem-resistant *A. baumannii* (CRAB) often results in nosocomial HAIs that can evolve into cluster infections; examples include bacteremia, pneumonia, and urinary tract infections. Furthermore, the mortality rate of patients who contracted CRAB is as high as 46%–63.9%.^{21,22} People at the highest risk include patients in hospitals, especially those who are receiving mechanical ventilation, have devices such as catheters, have open wounds from surgery, or are in ICUs, have prolonged hospital stays. In the United States, *Acinetobacter* infections rarely occur outside of health care settings,⁴ which is consistent with the findings of the present study. However, immunocompromised individuals and those with chronic lung disease or diabetes may be more susceptible to *Acinetobacter* infections.⁴ Studies from Taiwan^{22,23} have indicated that from November 2009 to February 2010, a cluster of MDR *A. baumannii* (MDRAB) colonization/infection was identified and investigated at an ICU of a Taiwan regional hospital. MDRAB was isolated from the sputum, central venous catheter, blood samples, pleural effusion, and bronchial washing fluid of nine patients. All patients received broad-spectrum antimicrobial therapy and ventilatory support. Among 38 swab cultures from ICU subjects, MDRAB was isolated from an Ambu bag, bed rails, a physician's desktop

computer keyboard, and a physician's notebook keyboard. All of these isolates carried the *bla*OXA-72 gene. The cluster was controlled after infection control measures were reinforced and compliance was monitored. Another local study²⁴ reported that CRAB infections in the ICU caused the ratio of medical care-related infection to rise from 18% in 2003 to 64% in the second quarter of 2010. This is consistent with the trend that the number of *A. baumannii* strains isolated from all infection sites including the urinary tract, respiratory tract, bloodstream, and surgical wounds has reached a prominent peak in 2010. A possible reason behind this phenomenon is the increase in MDRAB caused by the excessive use of postline broad-spectrum antibiotics; this problem has greatly limited the antibiotic options for patient treatment. Therefore, strict antibiotic prescription control is the most critical factor in preventing further drug resistance in *A. baumannii*. Another prominent epidemiological characteristics of the current study is that from 2008 to 2019, the number of isolates isolated from all infection sites including the urinary tract, respiratory tract, bloodstream, and surgical wounds has exhibited a gradually decreasing trend. A possible reason behind this is that proactive nosocomial infection control measures taken by large Taiwanese medical centers may have resulted in the effective control of *A. baumannii* or MDRAB outbreaks involving clinical infections in wards; this in turn prevents further spread of infection.

A. baumannii has become a major hospital pathogen because of its ability to resist desiccation, disinfectants, and major antimicrobials.²⁵ CRAB is arguably the most difficult to treat Gram-negative microorganism because of its high capacity for multidrug resistance. Currently, a substantial proportion of *A. baumannii* isolates are carbapenem resistant, extensively drug resistant, or even pandrug resistant.²⁶ CRAB causes substantial morbidity and mortality, with mortality rates for the most common CRAB infections (i.e., hospital-acquired pneumonia and bloodstream infections) approaching 60%.² Carbapenem resistance rates in *A. baumannii* have exceeded 70% in some parts of the world,²⁷ as noted in the current study. Carbapenem resistance rates in *A. baumannii* are 74.2% during COVID-19 pandemic between January 2020 and December 2020 in Taiwan. This is significantly higher than the rates for carbapenem-susceptible *A. baumannii* infections.²⁸ Within a hospital setting, MDRAB may be spread through medical personnel or contaminated environment or medical devices.²⁹ The risk factors for contracting *A. baumannii* infections include severe illness with experience of infections or septicemia, prolonged usage of artificial respirator, presence of *A. baumannii* colonization, and a prolonged ICU stay.³⁰ Therefore, the current study recommends correct hand-washing routine and maintaining adequate personal

hygiene for tackling *A. baumannii* infections. Patients infected with pan-drug-resistant *A. baumannii* should be moved to the quarantine ward for further care and placed in different quarantine zones. To reduce or eliminate MDRAB, and in turn enhance the overall health care quality, professional medical personnel or caregivers must prevent spreading the virus by using facial masks, gloves, and isolation gowns according to the “Standard Precautions” and “Contact Precautions” established by the Taiwan CDC.

This study has several limitations. First, the Taiwan CDC’s infectious disease statistics (TNIDSS) includes only basic data of infection sites of patients with *A. baumannii*, resistance strain number, and provides no clinical data. Therefore, this study could not compare clinical data between patients in terms of their differences or trends. Second, the TNIDSS database does not include information on *A. baumannii* genotypes or strains, precluding the analysis of the *A. baumannii* strains in Taiwan or a comparison between *A. baumannii* strains in Taiwan and other countries. Third, no antibiotic data against *A. baumannii* strains were available; thus, the interaction between *A. baumannii* strains and those with antibiotics was not compared. This study has the advantage of using diverse data provided by Taiwan’s public sector on its online platform (including the initial version of the platform). This open platform has stored all historical data that researchers can use to conduct statistical analyses or create academic value. Such data are worth exploring to expand the monitoring of infectious diseases and their characteristics, thereby continually increasing the capacity of scientific research.

CONCLUSION

This study is the first in Taiwan to analyze the bacterial characteristics and trends of patients with *A. baumannii* and drug-resistant *A. baumannii* from 2008 to 2019. This 12-year retrospective study revealed that high rates of CRAB continue in ICUs in Taiwan. This is a serious public health concern that requires the government, hospitals, and medical practitioners to collaborate in medical care to reduce the infection and resistance rate of *A. baumannii*. This information will be useful for policy-makers and clinical experts in directing prevention and control measures. This study highlights the importance of longitudinal and geographically extended studies to understand the implications of health care-related transmission of *A. baumannii* infection in the Taiwanese population.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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