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Original Article

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Carbapenem-resistant *Acinetobacter baumannii* Outbreak in a COVID-19 Isolation Ward and Successful Outbreak Control with Infection Control Measures

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ABSTRACT

Background: Even amid the coronavirus disease-19 (COVID-19) pandemic, the spread of multidrug-resistant bacteria and infection control are still important tasks. After recognizing the carbapenem-resistant *Acinetobacter baumannii* (CRAB) outbreak that occurred in the isolation room for COVID-19, we would like to introduce what infection control measures were implemented to eradicate it.

Materials and Methods: All COVID-19 patients with CRAB in any specimen admitted to the COVID-19 isolation ward of the tertiary hospital in Korea from October to November 2021 were analyzed.

Results: During the outbreak, 23 patients with COVID-19 and CRAB infections were identified. The index case was an 85-year-old female referred from a long-term care facility. CRAB was identified in sputum culture in most patients (91.3%). The CRAB outbreak occurred mainly in the rooms around the index case. Environmental cultures on the floor, air inlet, air outlet, and window frame of the rooms were performed. The antimicrobial resistance patterns of CRAB from patients and the environment were identical; whole-genome sequencing analyses revealed isolated clonality. Infection control measures with enhanced environmental cleaning using 1,000 ppm sodium hypochlorite and phenolic compounds, enhanced hand hygiene, additional education, and mandatory additional gowning and gloving of COVID-19 personal protective equipment (PPE) were applied on 29 October. No CRAB infection cases occurred from 2 November for two weeks.

Conclusion: In addition to applying PPE and COVID-19 precautions in COVID-19 isolation wards, adhering to strict contact precautions along with environmental control can help prevent the spread of multidrug-resistant bacteria.

Keywords: COVID-19; *Acinetobacter baumannii*; Outbreak; Environmental cleaning

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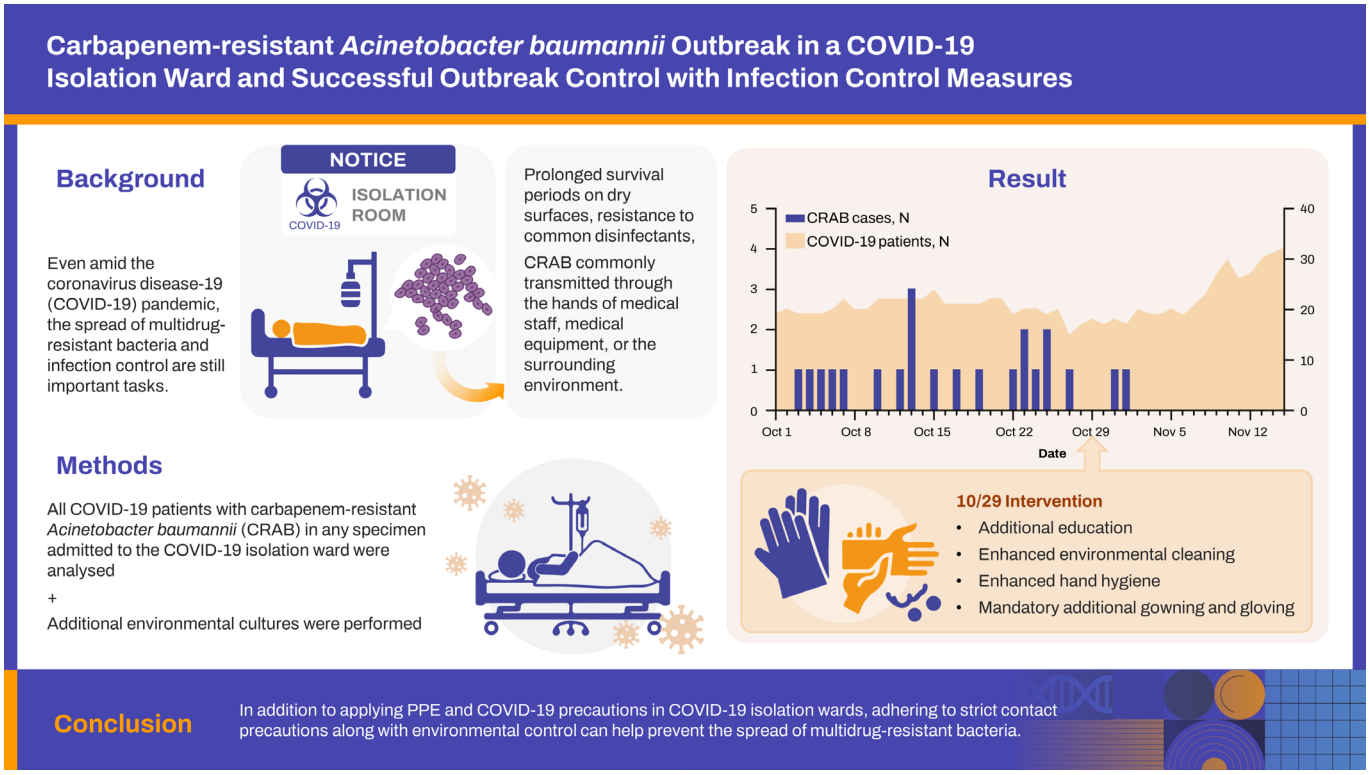
GRAPHICAL ABSTRACT



INTRODUCTION

Coronavirus disease 2019 (COVID-19) has become a global health concern since its discovery in December 2019. And in patients with COVID-19, multidrug-resistant organisms (MDROs) colonization is becoming a problem due to prolonged hospitalization, transfer from a long-term care facility, and exposure to antibiotics [1, 2]. In addition, MDROs are themselves a risk factor for infection and can result in the unrecognized spread of MDROs to non-colonized persons, so infection control in COVID-19 patients is an important issue [3-5]. However, after the coronavirus pandemic, several studies show conflicting results regarding MDRO rate. Some literature reports that MDRO colonization has decreased as infection control has become stricter [6], but some literature also reports that proper management is not possible due to lack of medical equipment, lack of infection control personnel, and exhaustion of medical staff-causing increase of MDRO [7].

Acinetobacter baumannii is a nosocomial pathogen mainly associated with healthcare-associated infection (HAI) and can cause secondary infections in COVID-19 patients, such as bloodstream infection or ventilator-associated pneumonia [8-12]. Carbapenem-resistant *A. baumannii* (CRAB) prevalence is increasing in COVID-19 patients, with studies reporting approximately 20% of cases [13]. The reason why we need to focus on CRAB among MDRO is because *A. baumannii* can contaminate hospital environments owing to its prolonged survival periods on dry surfaces and resistance to common disinfectants [14-16]. Therefore, the outbreak of HAIs with CRAB significantly threatens hospitalized COVID-19 patients.

Most COVID-19 patients are admitted to isolation rooms for airborne precautions, and healthcare workers wear personal protective equipment (PPE) such as respirators, face shields, goggles, gloves, and gowns according to stipulated guidelines [17, 18]. Strict precautions are applied to hospitalized COVID-19 patients; however, MDRO outbreaks may still occur. Although guidelines for infection control measures to reduce MDRO transmission in hospitalized patients exist [16], additional measures helpful in controlling the MDRO outbreak in COVID-19 isolation wards remain unclear. This study reports a CRAB outbreak in a COVID-19 isolation ward and its successful eradication using enhanced environmental cleaning and additional gowning and gloving.

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MATERIALS AND METHODS

1. Study setting

This study was performed in a 3,000-bed tertiary care medical center in Seoul, Korea, between October and November 2021. The isolation ward is an independent space in the hospital and had 32 beds dedicated to patients with severe COVID-19 (**Fig. 1**). The isolation ward consisted of 20 single rooms with middle doors and 3 four-person rooms without middle doors. All doors, including the middle door, were opened and closed manually. When entering the isolation room, all patients underwent sputum and blood culture as baseline studies. Culture was repeated if fever persisted for more than 3 days, inflammatory marker increased for no particular reason, or worsening of infection was suspected. Active surveillance for CRAB was not conducted during study period.

All COVID-19 patients with CRAB in any culture specimen admitted to the COVID-19 isolation ward during the study period were analyzed. Data on patient demographic and clinical characteristics, transfer history within the isolation ward, invasive procedures, and involved healthcare workers were obtained from electronic medical records. COVID-19 severity was classified as mild (without oxygen demand or application of nasal cannula), moderate (with the application of high-flow nasal cannula [HFNC] or mechanical ventilation), and severe (with the application of continuous renal replacement therapy or extracorporeal membrane oxygenation).

2. Ethics statement

This study was approved by the institutional review board (IRB) of Severance Hospital. The requirement for written consent from patients was waived, as the study had a retrospective design (IRB authorization No. 4-2021-1543).

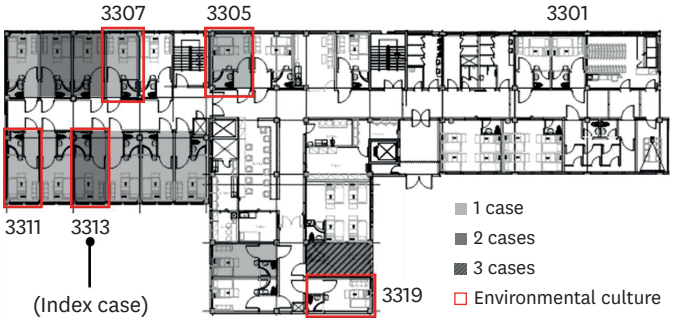

Figure 1. Floor plan of isolation ward with *Acinetobacter baumannii* outbreak.
Hospital rooms are numbered counterclockwise starting from room 3301. The top view colour indicates the number of outbreak cases, and the area marked with a red rectangle indicates the locations where environmental cultures were conducted.

3. Epidemiological and environmental investigation

At the end of October, the infection control office recognized the CRAB outbreak and conducted an epidemiological investigation and enhanced infection control measures. Since the index case was a patient in a single room who referred from a long-term care facility and never got out of bed on his own, environmental transmission was suspected. Therefore, along with strengthening environmental management, environmental culture of the isolation rooms where patients with CRAB from any specimen were hospitalized was performed. The environmental culture was obtained using swabs in a grid pattern of 10 × 10 cm on the surfaces and commonly used inspection items, such as ventilator monitors, bed rails, suction preparation tables, door handles, computer keyboards and monitors, and nursing carts. Moreover, additional environmental cultures on the floor, air inlet, air outlet, and window frame of the rooms were conducted (**Fig. 1**), in consideration of propagation through air dispersal. All but three patients were in bed-ridden status and could not use the bathroom in the isolation room, investigation regarding water supply was not conducted.

4. Intervention

The infection control measures were enhanced according to the in-hospital guidelines. First, environmental cleaning was enhanced using a disposable towel with 1,000 ppm sodium hypochlorite and phenolic compounds more than twice daily. The floors, door handles, armrests, and tables in the hospital rooms, all of which are mostly in contact with patients and medical personnel, were frequently disinfected. When a patient exits or moves from room to room, environment protection agency registered disinfectants were sprayed twice at 20-min intervals or once after 20 min of UV-C sterilizer spray for 20 min, and a wipe set was used to disinfect the environmental surface. Wearing gowns and gloves over PPE when entering each patient room has been changed from recommended to mandatory, and enhanced hand hygiene (required use of hand sanitizer before and after entering the hospital room) and additional educations for health workers were applied from 29 October, 2021.

5. Microbiology

Bacterial identification and antimicrobial susceptibility tests were performed using the VITEK 2 system

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(bioMérieux, Hazelwood, MO, USA). The antimicrobial susceptibility test results were interpreted according to the 2018 guidelines of the Clinical and Laboratory Standards Institute [19]. Resistance to carbapenem was defined as a minimum inhibitory concentration (MIC) of ≥8 μg/mL to imipenem or meropenem.

6. Whole-genome sequencing (WGS) analysis

WGS was performed to determine the genetic relatedness between the isolates. We performed WGS on some strains (total of 10 strains) acquired from patients. Genomic DNA was extracted from the strains using a Wizard Genomic DNA Purification Kit (Promega, Madison, WI, USA). Next, the DNA was sheared using a g-TUBE apparatus (Covaris, Inc., Wouburn, MA, USA), and the fragments were purified using 0.45 × of the final volume of washed Agencourt AMPure XP magnetic beads (Beckman Coulter, Inc., Brea, CA, USA).

RESULTS

1. Number of cases with CRAB

During the outbreak period, 23 patients with COVID-19 and CRAB infection were identified. In September, no CRAB was cultured in the isolation ward. The first CRAB in the isolation ward appeared in a culture performed on October 3. The index case was an 85-year-old female patient referred from a long-term care facility for mechanical ventilation after intubation on 11 September 2021. CRAB was identified in the sputum, neck wound swab, and coccyx sore swab culture of the patient on 3 October, which was the 22nd day of hospitalization and mechanical ventilation. Following its identification in the index case, CRAB with similar susceptibility patterns was identified in more than one patient almost daily (**Fig. 2**). All the isolates were resistant to meropenem (MIC ≥8 μg/mL).

2. Clinical characteristics of patients with CRAB infection

The mean age of the patients with CRAB infection was 72.9, and 14 (60.9%) were male. In most patients (91.3%), CRAB was identified in sputum culture; CRAB was identified in blood and sputum and blood (simultaneously) cultures of two and four patients, respectively. Most patients received an HFNC (26.1%) or mechanical ventilation (60.9%). CRAB was confirmed on a mean day 13.3 of hospitalization (**Table 1**). Antimicrobial susceptibility test to other antibiotics were also performed. CRAB isolated from two cases (accounting for 8.7%) exhibited resistance to amikacin or polymyxin E, which are often added as combination therapies against CRAB infection (**Table 2**) [20].

3. Outbreak investigations and interventions

A. baumannii commonly causes monoclonal outbreaks related to an environmental source [14, 15]. Since CRAB antimicrobial susceptibility test results were similar, a clonal spread was considered. No specific epidemiological factors associated with the outbreak were identified

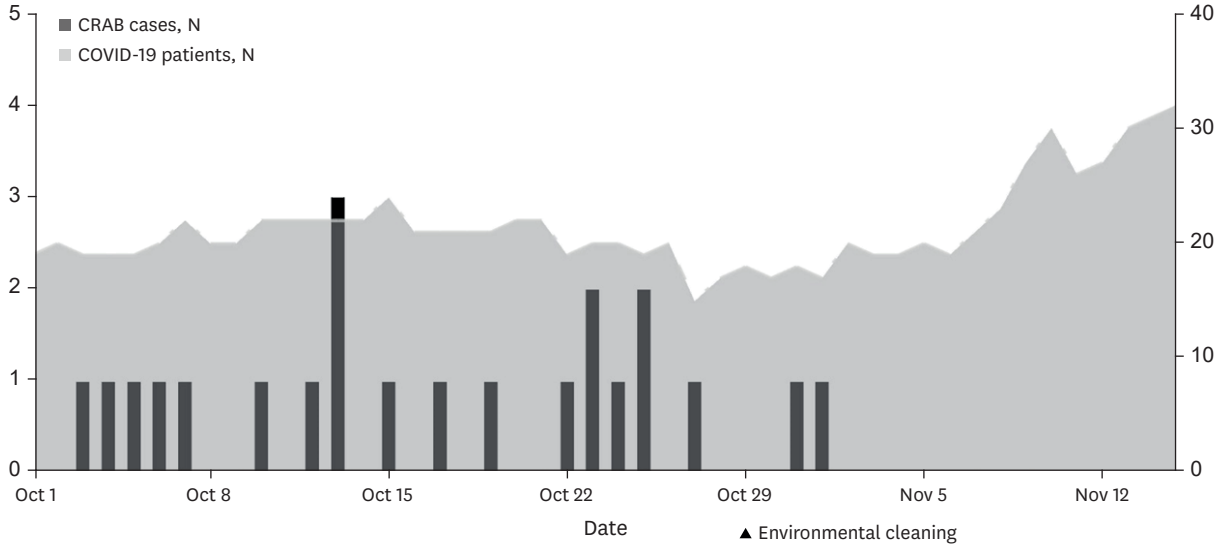

Figure 2. Daily number of cases with carbapenem-resistant *Acinetobacter baumannii* during the outbreak period.
The daily number of cases is displayed as a dark gray bar with the number of people on the left Y-axis, and the total number of patients admitted to the isolation ward is displayed as a light gray line on the right Y-axis.

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Table 1. Baseline characteristics of patients with carbapenem-resistant *Acinetobacter baumannii* acquisition

Characteristic	N
Gender, male	14 (60.9)
Age, years	72.9 (±13.8)
Initial specimen	
Sputum	21 (91.3)
Blood	6 (26.1)
Urine	1 (4.3)
Skin swab	1 (4.3)
Severity	
Mild (room air or nasal cannula)	3 (13.0)
Moderate (HFNC or ventilator)	18 (78.3)
Severe (CRRT or ECMO)	2 (8.7)
Duration from admission to CRAB isolation, days	13.3 (±11.0)
Vaccination	8 (34.8)
Underlying disease	
Hypertension	16 (69.6)
Diabetes mellitus	10 (43.5)
Cardiovascular disease	8 (34.8)
Chronic lung disease	4 (17.4)
Solid cancer	6 (26.1)
Hematologic malignancy	2 (8.7)

Data are presented as mean ± standard deviation or number (%) of patients, unless otherwise indicated.
HFNC, high flow nasal cannula; CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation; CRAB, carbapenem-resistant *Acinetobacter baumannii*.

Table 2. Antibiotic resistance test of *Acinetobacter baumannii*

Antibiotic	N
Amikacin	2 (8.7)
Gentamicin	3 (13.0)
Colistin	2 (8.7)
Minocycline	0
Tigecycline	6 (26.1)

Data are presented as the number (%) of patients unless otherwise indicated.

by preliminary investigations; therefore, WGS and the possibility of environmental contamination were evaluated.

The CRAB outbreak occurred mainly in the wards around the index case (**Fig. 1**), and environmental culture was conducted in the areas marked with a red rectangle where the room used by the case patient on 2 November. Given that environmental cultures were conducted four days after enhanced environmental cleaning, CRAB was not isolated from the instruments. However, a large number of *A. baumannii* strains were cultured around the air outlets and floors (**Table 3**). In addition, for CRAB cultured from patients admitted to the 3305, 3307, 3309, 3310, 3317, and 3320 rooms, WGS showed a genetic correlation high enough to be considered a CRAB outbreak, as an identical clonal spread was observed, except for the CRAB identified in the catheter of a patient admitted to room 3309 on 25 October.

On 29 October, environmental disinfection was conducted. Infection prevention education was repeated to the staff responsible for cleaning and disinfection. Environmental cleaning of medical instrument surfaces within the isolation room and other high-touch surfaces was performed by the attending nurses and cleaning staff. Adherence to hand hygiene and additional gowning and gloving was taught and monitored by infection control practitioners. These measures were applied by referring to the additional implementation method used following an MDRO outbreak in the hospital.

After applying the interventions for infection control, no additional CRAB cases were observed for two weeks from 2 November 2021 despite the overall number of patients admitted to isolation wards not decreasing (**Fig. 2**).

DISCUSSION

In a recent study, approximately 20% of secondary bacterial infection were observed in COVID-19 patients; In particular, secondary infections due to CRAB which can spread through environmental space have been associated with poor outcomes due to fewer treatment options [21-23]. Environmental transmission in isolated spaces such as isolation rooms or intensive care units is

Table 3. Result of environmental culture

Ward	Space	Pathogen
3305	Floor	(1) Many colonies of *Klebsiella pneumoniae*, (2) Few colonies of *Enterococcus faecium*
	Window frame	No growth for 48 h
	Air outlet	1 CFU of *Bacillus subtilis*
	Air inlet	(1) 7 CFUs of *Enterococcus faecium*, (2) 4 CFUs of *Bacillus mojavensis*
3307	Floor	Many colonies of *Acinetobacter baumannii*
	Window frame	(1) 1 CFU of *Bacillus subtilis*, (2) 1 CFU of *Bacillus simplex*
	Air outlet	Few colonies of *A. baumannii*
	Air inlet	Many colonies of *A. baumannii*
3311	Floor	Many colonies of *A. baumannii*
	Window frame	No growth for 48 h
	Air outlet	Many colonies of *A. baumannii*
	Air inlet	Many colonies of *A. baumannii*
3313	Floor	Many colonies of *A. baumannii*
	Window frame	Many colonies of *A. baumannii*
	Air outlet	Many colonies of *A. baumannii*
	Air inlet	Many colonies of *A. baumannii*
3319	Floor	1 CFU of *Staphylococcus epidermidis*
	Window frame	(1) 3 CFUs of *S. epidermidis*, (2) 1 CFU of *Paenibacillus* sp.
	Air outlet	No growth for 48 h
	Air inlet	Many colonies of *K. pneumoniae*

CFU, colony forming unit.

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already well known during the COVID-19 pandemic [10, 11, 24]. Many studies have attempted to reduce nosocomial spread by enhancing environmental cleaning or no-touch technologies, self-disinfecting surfaces, and monitoring strategies [25-27]. Although guidelines for managing infection control measures to reduce MDRO transmission have been established, guidelines for managing infection control measures to reduce *A. baumannii* transmission, commonly spread throughout the environment, are yet to be established [15, 28]. In addition, *A. baumannii* colonization is a relative risk of actual infection [24], and considering the frequent movement into hospital rooms during the COVID-19 quarantine period, studies on methods or guidelines for preventing *A. baumannii* spread in COVID-19 patients are required.

The isolation ward in our hospital is an independent space and was created to treat air-borne diseases such as COVID-19. It can accommodate up to 32 people, 20 of which are single rooms with a middle door and a separate bathroom. The door was operated manually, and plastic gloves and gowns were placed both inside the middle door and outside the patient's room. All patients underwent sputum and blood culture upon hospitalization, and the first CRAB was confirmed through sputum, neck wound, and sore swab culture in the index case. Considering that CRAB has never been cultured in patients admitted to the isolation ward in September, that the index case was transferred directly from a long-term care facility to the isolation ward, and that the carbapenem resistance rate of *A. baumannii* at the local hospital is over 80% [29], initial CRAB believed to be originated from outside the hospital. And all patients except three were in near bed-ridden status and were unable to use the bathroom or middle door in their rooms, transmission would have occurred through the environment or healthcare workers.

As a hospital exclusively for critically ill patients, a ventilator or HFNC is applied; thus, there were no cases of patients moving out of their rooms. Nevertheless, a CRAB outbreak occurred, and WGS confirmed its clonal spread. However, this study demonstrates that simple environmental cleaning, education, and precautions can effectively eradicate the outbreak.

Although these results are encouraging, this study had several limitations. First, as the hospital is a tertiary hospital in Korea, patients were mainly those with severe cases or those hospitalized for long-term care; therefore, a bias may have ensued in patient selection. In addition, the study was conducted only on patients with confirmed CRAB infection rather than performing active surveillance of all hospitalized COVID-19 patients. The same clonal spread was confirmed through WGS, and through environmental culture, the possibility of transmitting the same clones remaining in the environment even after general disinfection was inferred. However, it is difficult to determine the specific route, as the clinician, air, or other routes are potential transmission routes. Moreover, as shown in most studies on MDRO propagation, predicting the efficacy of simple interventions, as in this study, is difficult because most hospitals have intensive care unit settings (a shared room), unlike the hospital setting in this study.

Nevertheless, this study established the possibility of CRAB propagation even in single-room isolation with negative pressure and middle door, the importance of environmental management, and the possibility of successful control or eradication with simple care.

In addition to applying PPE and COVID-19 precautions in COVID-19 isolation wards, adhering to strict contact precautions along with environmental control can help prevent the spread of multidrug-resistant bacteria.

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Conflict of Interest

JYC is editorial board of Infect Chemother; however, he did not involve in the peer reviewer selection, evaluation, and decision process of this article. Otherwise, no potential conflicts of interest relevant to this article was reported.

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Author Contributions

Conceptualization: KHL. Data curation: KHL. Formal analysis: KHL. Investigation: OMK, EJY, HML. Methodology: KHL. Project administration: JYC. Resources: JYC. Supervision: JYC. Validation: JYC. Visualization: KHL. Writing - original draft: KHL. Writing - review & editing: JK, JAL, CHK, JHK, SJJ, NSK, JSY, JYA, JYC.

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