

Monitoring Multidrug-Resistant *Acinetobacter baumannii* Infections in the Neurosurgery ICU Using a Real-Time Surveillance System

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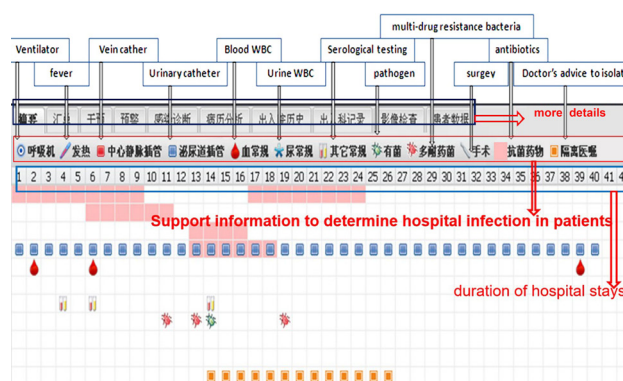
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Abstract

Multidrug-resistant *Acinetobacter baumannii* (MDR-AB) infections are becoming increasingly common. The Real-Time Nosocomial Infection (NI) Surveillance System (RT-NISS) was used to monitor MDR-AB NI in intensive care units (ICUs) to prevent NI outbreaks. Therefore, the RT-NISS was used in the current study to monitor MDR-AB infections in a neurosurgery ICU. Clinical interventions, including recommended antibiotics, bacterial distribution in the patient analysis, and bed adjustments, were carried out based on the monitoring results. The RT-NISS was also used to monitor clinical data, implement, and provide training on NI control. The RT-NISS detected a potential cluster of XDR-AB when five patients admitted to the neurosurgery ICU were tested positive for AB between 11 and 17 June 2019. Only two infected cases originated in the hospital, and there was no NI outbreak. The hospital Infection Control Department took appropriate measures to prevent cross-infection; specifically, an epidemiologic investigation and environmental assessment were conducted, and NI prevention and outbreak management training was provided. In summary, the RT-NISS enhanced the timeliness and efficacy of NI control and surveillance in a neurosurgery ICU.



In order to prevent NI outbreaks, the Real-Time Nosocomial Infection (NI) Surveillance System (RT-NISS) was employed to monitor MDR-AB NI in critical care units (ICU). Based on the monitoring data, clinical actions such as required antibiotics, bacterial distribution in the patient analysis, and bed changes were carried out. In a neurosurgery ICU, the RT-NISS improved the timeliness and efficacy of NI control and surveillance.

Key words: *Acinetobacter baumannii*, intervention, nosocomial infection, neurosurgery, real-time monitoring system

Introduction

Acinetobacter baumannii (AB), a non-glucose fermenting Gram-negative bacillus, is common in natural and hospital environments and can survive for a long time on table surfaces, clothing, and medical instruments (Kramer et al. 2006). In addition, AB is a nosocomial pathogen with poorly defined reservoirs outside the clinical environment (Howard et al. 2012). In recent years, advances in infection control have been achieved; however, AB infections are still globally dis-

tributed among patients in intensive care units (ICUs) (Strich and Palmore 2017). The incidence of infections with multidrug-resistant *A. baumannii* (MDR-AB) and extensively drug-resistant *A. baumannii* (XDR-AB) are on the rise (Kollef et al. 2008; Basri et al. 2015; Strich and Palmore 2017). Ineffective treatment of patients with AB infections increases the mortality rate four-fold compared with other infections (Kollef et al. 2008). AB accounts for 4% of all meningeal and shunt-related infections among neurosurgery patients, and the mortality rate of hospital-acquired meningitis in neurosurgery

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patients is as high as 31% (Basri et al. 2015). The epidemic nature of hospital MDR-AB outbreaks is challenging to control because AB is an opportunistic pathogen mainly associated with hospital-acquired infections (Wilks et al. 2006; Landelle et al. 2013). AB is frequently related to aquatic environments and has been shown to colonize in high numbers from the respiratory and oropharynx secretions of infected individuals (Turton et al. 2006; Sebeny et al. 2008). In an epidemiologic study involving 11,546 patients with XDR-AB cultures, 88.7% of cases had antibiotic exposure, while 81% had hospital or long-term care admissions in the prior 90 days (Fitzpatrick et al. 2021). Among these patients, the 30-day and one-year mortality rates were 23.5% and 48.8%, respectively (Fitzpatrick et al. 2021). A 12-year epidemiologic study conducted in China showed that AB infection control in hospitals is difficult due to patients' complex and diverse genetic backgrounds (Jiang et al. 2021). Nevertheless, active surveillance screening can help prevent outbreaks (Wilks et al. 2006). Traditional NI surveillance includes case reporting by physicians and retrospective analyses by the hospital Infection Control Department (ICD); however, these approaches have some disadvantages, including insufficient reporting, poor early detection of infection outbreaks, and inadequate control of NIs. The Real-time Nosocomial Infection Surveillance System (RT-NISS) has been increasingly used to overcome these shortcomings (Huang et al. 2010).

We used hospital data to demonstrate RT-NISS functions. On 17 June 2019 the ICD identified suspicious NI outbreaks using the RT-NISS in a tertiary general teaching hospital with 1,900 beds and initiated an epidemiologic investigation. The significance of RT-NISS in preventing nosocomial outbreaks was assessed in the current study.

Experimental

Materials and Methods

RT-NISS. Bacterial colonization refers to the isolation of bacteria from a patient without symptoms of infection and is a prerequisite for active infection. An infection is defined as the presence of bacteria that cause pathologic changes, albeit to different degrees (Correa and Fortaleza 2019; Arzilli et al. 2022). As defined by the Chinese Ministry of Public Health in 2009, hospital outbreaks require at least three infectious cases with the same pathogenic agent in the same hospital department within seven days (The Ministry of Public Health 2009). The RT-NISS (the Xinglin Hospital Infection Real-time Monitoring System, V12.0, <http://www.xinglin-tech.com>) was used to extract clinical data from the hospi-

tal information system (HIS) and hospital laboratory information system (LIS), including the use of ventilators and catheters, body temperature, blood, and urine test results, procalcitonin levels, bacteria identification, number and type of surgeries, antibacterial agents, and patient isolation. Thus, data on patients who might have been diagnosed with an infection were used to provide a warning to clinicians and ICD staff, and determine the source of infection in a timely fashion.

In addition, real-time surveillance data were collected to guide clinical practice, and an interactive platform was developed to establish communication between the clinical staff and the ICD to improve case reporting, patient isolation, and intervention measures. Therefore, with basic and epidemiologic information, the ICD staff and clinicians work together to determine the source of NIs. The RT-NISS was used to extract clinical data from the HIS and LIS, including central venous catheters and antibacterial agents, pathogenic bacteria, and underreporting rates, which were analyzed by the ICD staff to confirm suspiciousness cases and guide clinical practice. A previous study showed that the specificity and sensitivity for diagnosing NIs in patients by the RT-NISS were 93.0% and 98.8%, respectively (Du et al. 2014).

Surveillance path of the RT-NISS. The surveillance path of the RT-NISS was as follows: NI-related information was achieved from the HIS, hospital LIS, and radiology information system by data access middleware, including ventilator use, fevers, central venous catheterization, urinary tract catheterization, routine blood test results, routine urine test results, other laboratory test results (e.g., procalcitonin), bacteria-positive cultures, multidrug-resistant (MDR) bacteria, surgery, antibacterial agents, and medical advice regarding isolation. In this way, the prognosis for patients with infections was generated to provide warning for the clinical medical staff and the hospital infection management staff, and detect occult hospital infection outbreaks in a timely fashion. The NI algorithm screening proceeded to send out outbreak and NI case alerts. The Chinese Ministry of Public Health defined hospital outbreaks in 2009 as at least three infection cases with the same pathogenic agent in the same hospital department within seven days (The Ministry of Public Health 2009). Algorithms were based on statistical process control (SPC). The alert threshold not only defined elementary threshold, which was according to the management standards promulgated by the Ministry of Public Health, but the alert was triggered when cases exceeded a threshold of ≥ 3 infections in two weeks on the same ward. The alert threshold was also based on past statistical variations of case frequency.

The SPC offers the possibility to monitor different types of statistical parameters, such as the incidence

count or rate, cumulative sums, or moving average. An outbreak database was set up in response to an outbreak alert, and clinical intervention was implemented to control the outbreak. In the absence of outbreak alerts, the surveillance ended. Assessments by infection control personnel (ICP) proceeded following NI case alerts. The surveillance ended if the ICP judges deemed no issues with the alerts. An NI database was set up if the ICP judges considered the alerts abnormal. Another path for NI case alerts or complicated NIs was discussing with physicians. The physician's platform differentiated the NI cases and entered the NI cases into a NI database. If the physician confirmed that the case was not an NI, the surveillance was ended. After the database was established, a hospital-wide NI analysis was performed, and NI-targeted surveillance data were collected. The details can be reviewed on the flowchart of NI cases and outbreak pre-warning and confirmation in the Du et al. (2014) study.

When it was shown that the same type of bacteria appeared in a department for a short period and >3 nosocomial infection cases were confirmed, it was suspected that NI outbreaks might occur, and clinical intervention should be arranged. The interaction platform constructed through the hospital infection real-time monitoring system was applied to realize the real-time report of infection cases, precise diagnosis, intervention, and feedback. In so doing, the special staff and clinicians involved in the diagnosis and control of infections work together and are aware of an occult hospital infection outbreak in a timely fashion.

Patient information. This study was conducted in our medical center, which is in the middle of China. Our hospital has 1,900 beds and five ICUs. The neurosurgical ICU has 17 beds with 450 patients per year. Large general hospitals must prevent infectious clusters. The current study results were intended to serve as a reference for other general hospitals. From 11–17 June 2019, a total of 42 patients were admitted to the neurosurgery ICU and included in the study. The infection rate was counted. When the outbreak alerts were sent out, 32 of the 42 patients had been discharged. The ten hospitalized patients were alerted of a suspicious outbreak. The clinical intervention was initiated to prevent the outbreak. The use of antibiotics was reviewed and adjusted. The distribution of the bacteria in patients was analyzed.

The Chinese Ministry of Public Health defined hospital outbreaks in 2009 as at least three infection cases with the same pathogenic agent in the same hospital department within seven days. After the clinical intervention, five of the ten patients with suspicious NI outbreak alerts were clinically diagnosed with a suspicious NI according to the management standards promulgated by the Ministry of Public Health. AB was detected in the sputum samples collected from these

patients. According to the diagnostic criteria of nosocomial infection, the other five patients were excluded in the absence of an outbreak. These five patients did not meet the diagnostic criteria, such as admission within 48 h, and no bacterial growth occurred in the cultures (The Ministry of Public Health 2009).

The Institutional Ethical Committee approved the project of our hospital (2020-Ethics Approval-No. 12). The study was proceeded following the ethical standards of the Helsinki Declaration, as revised in 2013. The patients were informed about the study's purpose and procedures and provided written consent forms.

Clinical and environmental microbiologic method. Bacterial antibiotic susceptibility analysis was performed using the minimum inhibitory concentration (MIC) method (Andrews 2001), and the results were judged according to the CLSI (2010) standard of the American Committee for Clinical Laboratory Standardization. Strains were tested for susceptibility to ampicillin/sulbactam, ceftazidime, cefepime, imipenem, gentamicin, tobramycin, ciprofloxacin, and sulfamethoxazole.

Thirty-six environmental samples were collected from staff hands, humidified liquid, curtains, stethoscope, water bottle stopper, and water bottle shell, injection pump, faucet, bed cup and water, water feeding syringe, the railing of bed, lift the patient board. Cotton swabs were densely coated on blood plates, and the blood plates were placed in an air environment at 37°C and cultivated for 48 h, after which the strains were identified by a mass spectrometer (Repizo et al. 2017). Environmental samples were kept, collected, and tested every day within one week after the hospital infection management workers intervened in the investigation.

Statistical analyses. Statistical analyses were performed using SPSS software (version 20.0) on real-time surveillance data.

Results

Based on RT-NISS warnings, the five patients diagnosed with suspected AB infections included four males and one female, with a median age of 62 years (46–84 years). Most patients were older and had received a combination of invasive surgery and antibiotics. The baseline characteristics of the five patients are shown in Table I. A monitoring procedure (Fig. 1) was initiated to identify the source, and path of the NIs and the RT-NISS and clinical intervention were used to confirm suspected cases.

Epidemiologic information. Based on the HIS data, the number of NIs showed that the alert rate for suspicious infections or outbreaks from 11–17 June 2019 was 11.9% (5/42), which remained constant with the rates in 2018 and 2019 (Table II). The outbreak alert

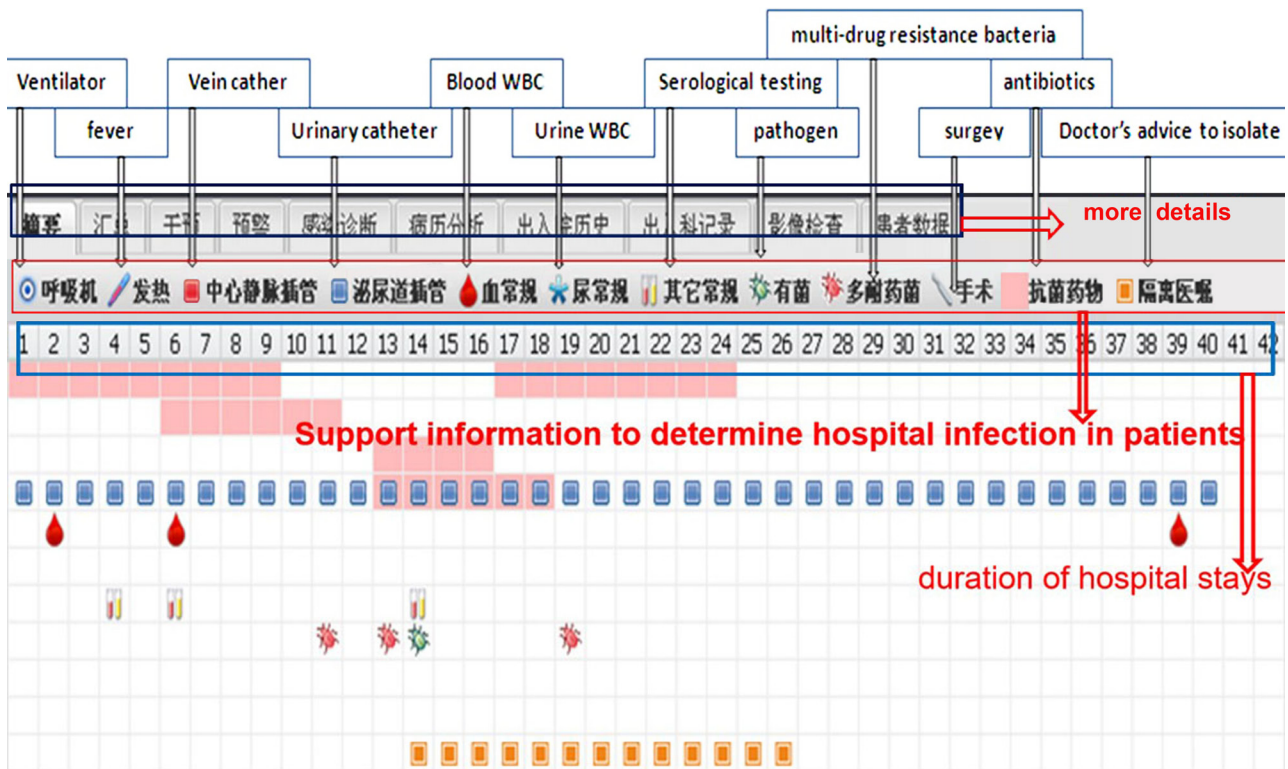


Fig. 1. This figure is a part of the visual time-series chart of inpatients shown by the software in use. Temporary clinical data shown were collected using a real-time nosocomial infection monitoring system. The data are displayed in different colors to facilitate comparison between patients. The symptoms represented in the system are displayed in Chinese and each symptom was translated into English, which was connected to the corresponding box with arrows to facilitate understanding. “More details” mean the detailed clinical data of the patients. The content of this interface only included the operation of patients with a suspected infection during hospitalization. The numbers 1–42 represent the duration of the hospitalization in days. A patient with an early warning appears as a red mark of multi-drug resistance bacteria on the warning interface. The possibility of a nosocomial infection outbreak was ruled out for multiple (≥ 3) patients, which was marked in red for multidrug resistance bacteria at any point in time. Because the warning interface contains a lot of patient information, the warning interface was not displayed completely.

rate was similar to other times throughout the year; thus, the RT-NISS could access the data quickly. Most patients with infections had severe injuries, including craniocerebral injuries and lung contusions, required intensive care, and increased the risk of cross-infections or secondary infections. Therefore, clinical examination confirmed suspicious cases to avoid underreporting and erroneous reports.

Case information. The five patients were clinically diagnosed and confirmed as below: one patient was confirmed to have a NI by the RT-NISS; one patient was suspected of having a NI by the RT-NISS and confirmed to be a NI by clinical interventions, and there were three patients with bacterial colonization originating in the hospital. The data excluded the possibility of an outbreak. The results of drug susceptibility testing are shown in Table III. The drug susceptibility test results suggested that the same pathogenic strain might be involved in the infections, potentially increasing the risk of an outbreak (Table III).

Case one. An 84-year-old man was admitted on June 9, 2019 with a craniocerebral injury and lung con-

tusion. The patient was treated with amoxicillin and levofloxacin for four days, then cefoperazone-sulbactam from June 13 until discharge from the hospital. He had an elevated white blood cell (WBC) count on June 13, and increased interleukin-6 and procalcitonin (PCT) levels on June 14. On June 13 XDR-AB was detected in a sputum sample, and rales were present bilaterally. Invasive surgery was performed, including chest drainage, a tracheotomy, and ventilator support. On June 13 he was reported to have a hospital infection in the lower respiratory tract.

Case two. A 46-year-old man was admitted on June 3, 2019 with a spontaneous cerebral hemorrhage. He was treated with amoxicillin from 3–15 June, piperacillin-sulbactam from 15–20 June, and ceftazidime from 20–30 June. On June 8 the patient was reported to have a lower respiratory tract infection associated with *Proteus mirabilis*. The symptoms persisted under continuous inspection. XDR-AB was detected on June 17 but did not cause any clinical symptoms. Urinary catheterization, a tracheotomy, and ventilator support were carried out. The final diagnosis was bacterial coloniza-

Table I
Baseline characteristics of the study population.

| | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 |
|---|------------------------|--------------------------------------|--------------------------------------|------------------------|---------------------|
| Age (y) | 84 | 46 | 62 | 65 | 57 |
| Gender | male | male | male | female | male |
| Bed code | J01 | 23 | 18 | 22 | J07 |
| Diagnosis | traumatic brain injury | spontaneous intracerebral hemorrhage | spontaneous intracerebral hemorrhage | traumatic brain injury | thalamic hemorrhage |
| Date of ICU admission | 9 June | 3 June | 1 June | 31 May | 14 May |
| Analyzed sample | sputum | sputum | sputum | sputum | sputum |
| Date of sample analysis | June 13 | June 17 | June 13 | June 11 | June 17 |
| Pathogen | AB (+++) | AB (+++) | AB (+++) | AB (++) | AB (++) KP (+++) |
| Date of tracheostomy | June 18 | June 6 | no | May 31 | May 17 |
| Duration of invasive mechanical ventilation | 3 | 30 | N/A | 8 | 23 |
| Antibiotic combination therapy | yes | yes | yes | yes | yes |
| NI or colonization | NI | colonization | colonization | NI | colonization |

AB – *Acinetobacter baumannii*, KP – *Klebsiella pneumoniae*

++, +++ mean semi-quantitative observation of stain under microscope according to the Health Industry Standards of the People's Republic of China (WS/T 499-2017), + means “occasionally”, ++ means “a small amount”, +++ means “medium amount”, ++++ means “a lot”

Table II
Suspected alert rates for infections or outbreaks in different periods.

| Periods | Number of suspected infections | Number of ICU patients | Rate of suspected infections | χ^2 | <i>p</i> -value |
|------------------------|--------------------------------|------------------------|------------------------------|----------|-----------------|
| 11–17 June 2019 | 5 | 42 | 11.9% | 0.267 | 0.875 |
| 20 May – 20 June 2018 | 6 | 38 | 15.8% | | |
| 20 April – 20 May 2019 | 6 | 41 | 14.6% | | |

Table III
Drug susceptibility of multidrug-resistant bacteria isolated from the patients.

| Antibiotics | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 |
|----------------------|--------|--------|--------|--------|--------|
| Ampicillin/sulbactam | R | R | R | R | R |
| Ceftazidime | R | R | R | R | R |
| Ceftriaxone | R | R | R | R | R |
| Cefepime | R | R | R | R | R |
| Imipenem | R | R | R | R | R |
| Gentamicin | R | R | R | R | R |
| Tobramycin | S | R | R | S | S |
| Ciprofloxacin | R | R | R | R | R |
| Levofloxacin | R | R | R | R | R |
| Sulfamethoxazole | S | R | R | S | R |

R – resistant, S – susceptible

tion because the culture results were inconsistent with the presence of sputum and symptoms of infection.

Case three. A 62-year-old man was admitted on June 1, 2019 with a spontaneous cerebral hemorrhage.

He was diagnosed with a lung infection upon admission and was given piperacillin-sulbactam and combination therapy (piperacillin-sulbactam and levofloxacin) on June 6. The testing of bacterial culture upon admission

was *Pseudomonas aeruginosa*. XDR-AB was detected in sputum for the first time on June 13 and *P. aeruginosa* infection was detected in the urine on June 14. There were no related symptoms during 6–13 June. The patient was treated with amoxicillin and amikacin from 13–16 June and piperacillin-sulbactam from 17–24 June. The patient was afebrile, and the WBC count was normal. Urinary catheterization and ventilator support were performed. *P. aeruginosa* did not become the dominant bacterium in the patient and did not cause symptoms. The final diagnosis was a bacterial colonization.

Case four. A 65-year-old woman was admitted on May 31, 2019 with a severe craniocerebral injury. Ventilator support was provided upon admission, followed by combination antibiotic treatment with amoxicillin, gentamicin, and levofloxacin. *Klebsiella pneumoniae* infection was detected in a sputum sample on June 5. On June 11, XDR-AB was detected. The body temperature increased, and the WBC count was elevated. Combination antibiotic treatment included cefoperazone-sulbactam and tigecycline, followed by meropenem and fluconazole. A bacterial infection was confirmed.

Case five. A 57-year-old man was admitted on May 14, 2019 with a thalamic hemorrhage. On 17 May the patient was reported to have a lower respiratory tract infection with *K. pneumoniae*. XDR-AB was detected in urine on May 19, *K. pneumoniae* was detected in a sputum sample on May 21, a small number of AB (++) was detected in a sputum sample on 16 June, and a medium number of *K. pneumoniae* (+++) was identified in a sputum sample on June 17 and 19. The patient's body temperature was normal during this period, and minimal phlegm was aspirated during suction. The patient was treated with amoxicillin, meropenem, tigecycline, cefoperazone-sulbactam, and amikacin. The final diagnosis was AB colonization.

Environmental samples. Case analysis showed a large number of MDR-AB strains in the ICU environment. To determine the source and path of infection, the ICD screened 36 environmental samples, including surfaces, hospital staff, and ventilators, of which 20 samples (55.5%) were contaminated. MDR-AB was detected in six samples, including a stethoscope, curtains, injection pump, a water faucet, and hands from two nurse workers. No new infections were detected during the one-week environmental samples tests in the following seven days.

Discussion

The early warning data on the five cases were acquired through the RT-NISS. RT-NISS monitored the infections in real-time. Outputting data on bacterial infections, suspected cross-infections, and the prevalence of outbreaks are exported from RT-NISS.

The RT-NISS captured the basic demographics about the patient and the corresponding epidemiologic information, which can lead to preliminary conclusions and save the investigation time. XDR-AB pneumonia remains a significant challenge in ICUs, and few drug treatment options are available for XDR-AB pneumonia treatment (Li et al. 2017). Ma et al. (2013) reported that mortality due to MDR and XDR-AB infections in China ICUs was 29% from 2011 to 2013. Indeed, the RT-NISS has an active role in providing accurate data to ICDs, diagnosing infections, and preventing outbreaks (Ma et al. 2013).

MDR-AB is rapidly becoming a global threat due to resistance to major classes of antibiotics (Nasr 2020). MDR-AB infections often occur in healthcare settings, especially in intensive care settings. *Acinetobacter* can survive for long periods on both wet and dry surfaces. *Acinetobacter* may also colonize or live in a patient without causing infection or symptoms, especially in tracheostomy sites and open wounds (Nwadike et al. 2014; Isler et al. 2018). The mechanisms underlying antimicrobial resistance in MDR-AB are complex, such as β -lactamase production, efflux pumps, decreased membrane permeability, and altered antibiotic target sites (Vrancianu et al. 2020). The control of MDR-AB has become a significant challenge in clinical practice (Asif et al. 2018).

According to the Hospital Infection Outbreak Control guideline (WS/T524-2016; The Ministry of Public Health 2009), there were no outbreaks in our hospital-based on this criterion. After intervention by the clinicians, only two cases were diagnosed with a NI, and it was not an outbreak within the hospital. The other three cases were regarded as colonization. It demonstrated that the system was used effectively to collect and analyze the clinical information of infected patients, help ICD confirm the diagnosis, actively treat the patients, and implement control measures (Du et al. 2014), such as antibiotic use instructions, analyzing the distribution of the bacteria within the patient, and contemplating bed adjustment. As demonstrated, data on the nosocomial transmission of drug-resistant bacteria can be retrieved accurately and rapidly with a real-time system, and variations in bacterial susceptibility to antibiotics can be determined (Chen et al. 2018). Compared with the original manual report, which generally requires confirmation of the infection and sending a report form to the Hospital Management Department, the system report can issue an early warning in real-time within 24 h and confirmation in the system (Huang et al. 2010). These data are compared with NI control targets established by health authorities to strengthen the actions of the ICD for preventing and controlling MDR bacterial infections. The system automatically extracts data and calculates the detection and infec-

tion rates and antimicrobial drug use in each hospital department every day (Leclère et al. 2017).

The RT-NISS was used to monitor infections in real-time. At the same time, the ICD promptly extracted clinical and epidemiologic information using the RT-NISS and instituted targeted measures to prevent infections and outbreaks (Zingg et al. 2015). The ICD systematically monitors the on-site status of clinical departments to avoid physician misconduct and initiates infection prevention and control measures, including epidemiologic investigations, patient isolation, environmental sanitation sampling, training, and measures to prevent and control multi-drug resistant bacteria. Moreover, the ICD should also cooperate with other departments to identify risk factors for spreading infections, control NIs, and promote the rational use of antibiotics (Zingg et al. 2015). The drug susceptibility data of pathogenic bacteria in the hospital, the bedside monitoring results of patients infected with XDR bacteria, and the prevention and control of drug-resistant bacteria spread can be obtained from the ICD monthly (Wieland et al. 2007). Each hospital department's pathogenic bacteria susceptibility data can be released every six months. Data collected daily and monthly by the RT-NISS on the number of NIs, use of antibacterial drugs, number of patients infected with XDR bacteria, drug susceptibility of pathogenic bacteria, and the prevalence and control of NI and NI outbreaks of drug-resistant bacteria can be shared between hospitals.

Furthermore, epidemiologic surveys and environmental sanitation sampling and identification should be carried out (Zingg et al. 2015). In our study, 55.5% of the environmental samples were contaminated, and MDR-AB was detected in five samples; however, no new infections were detected in the following seven days after the hospital infection management workers began to intervene in the investigation. This finding confirms that RT-NISS and the ICD can cooperatively monitor and prevent NIs in the hospital to some degree.

The research limitations of this study were as follows. First, the system generated false alarms; thus, an effective and reproducible framework is needed to evaluate and compare these algorithms. The computer screening algorithm did not include medical records; thus, the terminology application may not be uniform. Second, polymerase chain reaction tests of the samples were not completed due to the lack of hardware equipment in the hospital, and the classification of bacteria was achieved from the microbiology laboratory. Bacterial resistance is generally only identified using the MIC method in routine clinical work due to the costs involved. The antibiotic susceptibility test method based on the MIC values can guide the treatment and control of infections macroscopically. However, without genotyping or phenotyping tests, this is not an accept-

able approach for accurately judging whether there is an infection outbreak cluster. Also, PCR detection from environmental swabs was not performed due to the cost, which might affect the apparent correlation between AB strains isolated from patients and the environment. Finally, no automatic alarm appeared when the specimens were limited, and the early warning standard was not reached.

Conclusions

In summary, the RT-NISS integrated with the clinical diagnoses made by physicians enhances the timeliness and effectiveness of NI control and surveillance. The universal significance should be researched and explored by multiple hospitals.

Data availability

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to the privacy of research participants.

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Author contributions

CB initiated and supervised the study. YZ and MN designed the study design. All authors participated in the clinical study and data collection. XF and TL conducted the analysis. YZ, YS, RD have written the manuscript. XH and CB have made critical revisions on the manuscript. All authors have read and approved the manuscript before submission.

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Conflict of interest

The authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication

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