

Research Article

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Investigation and control of a suspected nosocomial outbreak of pan-drug resistant *Acinetobacter baumannii* in an intensive care unit

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Abstract: *Acinetobacter baumannii*, a non-fermenting Gram-negative bacterium, is a common pathogen in intensive care units (ICU) that is easily spread through contact and can cause nosocomial outbreaks. This study investigated the risk factors associated with outbreaks of pan-drug resistant *Acinetobacter baumannii* (PDR-Ab) infection by studying a suspected nosocomial outbreak in a comprehensive ICU in a teaching hospital in China, and discusses the effectiveness of current prevention and control measures.

Pathogen detection methods involving pulsed field gel electrophoresis (PFGE) were employed to survey patients infected or colonized with PDR-Ab. An epidemiological investigation was conducted to determine the risk factors for infection or colonization with PDR-Ab between 1 October 2014 and 16 January 2015.

The rate of PDR-Ab infection in the ICU was higher during the period from 1 October 2014 to 16 January 2015 than it was between 1 October 2013 and 16 January 2014. Only two cases were confirmed to have the same genotype. Risk factors were explored and the rate of infection was found to be controlled by interventions targeting these risk factors.

A decrease in the number of infections was observed after multiple prevention and control measures were implemented, preventing the outbreak of a nosocomial infection.

Keywords: *Acinetobacter baumannii*; Bacterial drug resistance; Epidemiology; Intensive care unit; Nosocomial infections; Pan-drug resistance

1 Introduction

Acinetobacter baumannii, a non-fermenting Gram-negative bacterium, is widely detected in nature, the hospital environment, and on human skin and other parts of the body. It is an opportunistic pathogen and has become a significant risk factor for nosocomial infections in intensive care units (ICUs) [1–3]. *A. baumannii* shows good survival under hygrothermal conditions and a high level of drug resistance. It commonly exhibits multiple-drug resistance (MDR, resistance to more than three different types of anti-infective drugs) or pan-drug resistance (PDR, resistance to the anti-infective drugs that are commonly used in the facility). The mechanisms of drug resistance in this organism are complex. *A. baumannii* can easily be spread through contact, thus leading to the spread of infections and potential outbreaks. There is therefore a need for programs to monitor and control nosocomial infections [4].

During a 5-day period, from Jan. 12 to 16, 2015, pan-drug resistant *A. baumannii* (PDR-Ab) was detected in sputum samples from three patients admitted to one comprehensive ICU in a teaching hospital in China. This constituted a suspected PDR-Ab infection outbreak and triggered an epidemiological investigation. Comprehensive prevention and control measures were undertaken to effectively control this cluster of PDR-Ab infections.

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2 Methods

2.1 Sample Selection

In total, 13 PDR-Ab infection cases were enrolled in this study, including three different types of cases:

- New cases: three new cases were detected from Jan. 12–16, 2015.
- Pre-existing cases: another four cases were detected from Oct. 1, 2014 to Jan. 11, 2015, among patients being treated in the hospital.
- Closed cases: six cases were detected from Oct. 1, 2014 to Jan. 11, 2015, among patients that had already been discharged.

2.2 Diagnostic criteria

PDR-Ab refers to *A. baumannii* that is resistant to all antibiotics [5]. The diagnostic criteria for nosocomial infections were based on the “Diagnostic criteria for nosocomial infection”, published by the Ministry of Health of the People’s Republic of China [6]. The diagnostic criteria for colonized patients were based on the “Expert consensus on the diagnosis, treatment and prevention of *Acinetobacter baumannii* infection in China” [7].

2.3 Epidemiological investigation and analyses

2.3.1 Investigation of temporal distribution

All 13 cases identified with PDR-Ab infection from Oct. 1, 2014 to Jan. 16, 2015 (including infection and colonization) were classified as the patient group. The control group consisted of patients identified with PDR-Ab infection in the same time period one year prior, from Oct. 1, 2013 to Jan. 16, 2014 (including infection and colonization). Chi-square tests were used to study the correlation between temporal distribution and PDR-Ab detection for these two groups.

2.3.2 Investigation of spatial distribution

All 13 cases identified with PDR-Ab infection from Oct. 1, 2014 to Jan. 16, 2015 (including infection and colonization) were classified as the patient group. Patients with infections from other MDR/PDR organisms in the same ICU

during the same time period formed the control group. This ICU was identified to have: 1. an attention unit (the room where most infection cases were detected); 2. an adjacent unit (two rooms next to the attention unit); and 3. other units (11 rooms). Fisher’s exact test was used to study the correlation between spatial distribution and PDR-Ab detection.

2.3.3 Investigation of respirators as a risk factor

All 13 cases identified with PDR-Ab infection from Oct. 1, 2014 to Jan. 16, 2015 (including infection and colonization) were classified as the patient group. Patients with other MDR/PDR infections in the same ICU during the same time period formed the control group. Fisher’s exact test was conducted to study the correlation between PDA-Ab detection and the use of a respirator.

2.3.4 Analysis of swab samples from the environment, throat and the hands of medical staff

On Jan. 20, 2015, the infection control department conducted swab sampling of surface environmental microorganisms, as well as swab sampling of the throats and hands of medical staff prior to disinfection in the ICU. The sampling methods followed those detailed in the appendix of the publication “Technical specifications for the disinfection in medical institutions” [8]. Environmental sampling was performed on the bed rails, bedside cabinets, bedside eating tables, the buttons on the respirator, the buttons on the nasogastric tube feeding pump, the buttons on the electrocardiography monitor, water from the sputum suctioning of PDR-Ab infected patients and adjacent non-PDR-Ab infected patients, and swabs from the throats and hands of the staff. In total, 132 samples were collected, and bacterial culturing revealed that five of the environmental samples had the same bacterial drug resistance profile as the sputum samples from the seven PDR-Ab patients.

2.4 Bacterial DNA homology analysis

Samples from the seven patients (new cases + pre-existing cases) and five environmental samples were sent to the Shanghai Municipal Center for Disease Control and Prevention. Bacterial DNA homology analysis was conducted using pulsed field gel electrophoresis (PFGE). Band matching was analyzed using BioNumerics (version 6.5)

software, and homology was determined in accordance with the Tenover rule [9].

2.5 Data analysis

SAS (version 9.2) software was used to perform chi-square tests, Fisher's exact tests, and other statistical analyses. Fisher's exact tests were used to study the possible correlation between the use of a respirator and PDR-Ab-positive culture tests. A P-value >0.05 was taken to indicate statistical significance.

2.6 Comprehensive prevention and control measures

2.6.1 Prompt reporting and unified commands

When the possible cluster of multiple PDR-Ab-infected patients was first detected, the situation was immediately reported to the vice president in charge of infection control at the hospital. A meeting concerning prevention and control was attended by the hospital directors and managers of the medical services, infection control department, microbiology department, ICU and respiratory departments. Specific measures for implementation were developed, the chain of command was unified, and the implementation of these measures was ensured.

2.6.2 Centralized treatment and isolation of patients with PDR-Ab infection

Three PDR-Ab infected patients were transferred to one room, and the remaining four patients were transferred to four different single rooms. Then the patients with PDR-Ab infections were strictly isolated from other patients. Isolation gowns were provided to medical staff at the entrance of the isolation ward. According to the guidelines, medical staff who entered the isolation ward were required to wear isolation gowns, surgical masks, hats, and clean or sterile gloves during all procedures and treatments. A team was

formed that was responsible for medical care in the isolation room. The head nurse in the ward was in charge of monitoring the isolation procedures.

2.6.3 Enhanced cleaning and disinfection management for the ward environment

In the isolation ward, cleaning and disinfection were conducted for all bed units, instruments and ward air. The cleaning staff were specially trained for the process of daily environmental disinfection. They were required to use towels soaked in chlorine solution (1,000 mg/L) to wipe the ward three times per day. The concentration of the chlorine solution was tested by the nurse before the solution was used. The disinfectant towels used for wiping were only used for one bed unit, before being re-soaked in chlorine solution (1,000 mg/L) for 30 minutes and dried for future use.

2.6.4 Other prevention and control measures

Other prevention and control measures included enhanced monitoring of hand hygiene, guidelines for antibiotic use,

Table 2: Relationship between PDR-Ab detection, hospital unit and the use of a respirator.

| | Patient group | Control group | P value |
|------------------------------|---------------|---------------|---------|
| Spatial distribution | 13 | 9 | 0.0585 |
| Attention unit | 8 | 2 | |
| Adjacent unit | 4 | 3 | |
| Other units | 1 | 5 | |
| Use (or not) of a respirator | 13 | 10 | 1.0000 |
| Yes | 8 | 6 | |
| No | 5 | 4 | |

Table 1: Comparison of the PDR-Ab detection rates during different time periods.

| Date | Total number of patients in the ward | Number of PDR-Ab-infected patients | Detection rate | P value |
|----------------------------|--------------------------------------|------------------------------------|----------------|---------|
| Oct. 1, 2014–Jan. 16, 2015 | 504 | 13 | 2.58% | 0.0362 |
| Oct. 1, 2013–Jan. 16, 2014 | 551 | 5 | 0.91% | |

and procedures for transferring patients and specimens and discharging patients.

Ethical approval: The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee.

Informed consent: Informed consent has been obtained from all individuals included in this study.

3 Results

3.1 Epidemiological investigation results

The temporal distribution of the PDR-Ab detection rates is shown in Table 1, indicating a significant increase over time. The spatial distribution of the number of patients for whom PDR-Ab was detected is shown in Table 2. The patients in the attention unit were more likely to be infected with PDR-Ab than other PDR bacteria, but this difference was not statistically significant. The relationship between the use of a respirator and PDR-Ab detection is also shown in Table 2. The results indicated that the use of a respirator does not increase the likelihood of detec-

tion of PDR-Ab compared with other MDR/PDR infections (Fisher's exact $P = 1.0000$).

3.2 Sampling results

A total of 132 samples were collected prior to disinfection. PDR-Ab was not detected in the 76 samples isolated from the throat swabs and hands of the ICU staff. The remaining 56 samples were collected from the environment and instrumental surfaces, including the bedside table, bedrail, water from sputum suctioning, and the buttons of nasogastric tube feeding pumps used in the case of PDR-Ab-positive patients. Five of these samples tested positive for PDR-Ab. Two PDR-Ab-positive patients occupied adjacent beds, and the samples collected from their bed rails were positive.

3.3 Bacterial DNA homology analysis results

The PFGE results are shown in Figure 1, and the results of matching analysis using BioNumerics software are shown in Figure 2. In Figure 2, the findings indicated that the PDR-Ab strains from patients No. 4 and No. 6 were completely homologous. The strains from patient No. 5 and the bed rails of patients No. 5 and No. 1 were also homologous. Lane 9 represents the strain isolated from the water from the sputum suctioning of patient No. 2. This strain was identified as *Elizabethkingia meningoseptica* by homology analysis, and PDR-Ab infection in this patient was ruled out.

3.4 Effects of the control measures on the cluster of MDR patients

After implementation of the aforementioned prevention and control measures, the infection control department of

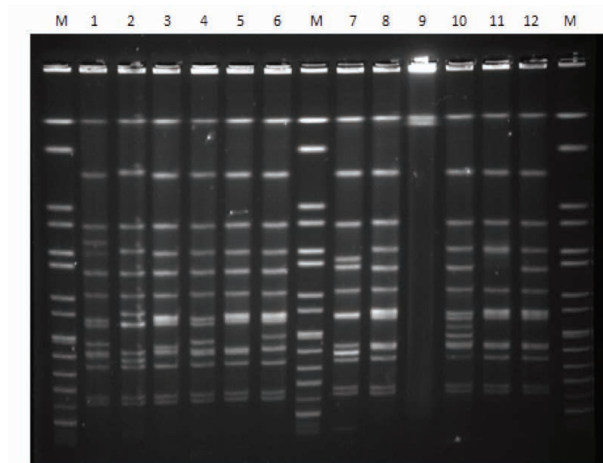


Figure 1: Pulsed field gel electrophoresis (PFGE) band images for samples from seven patient cases and five environmental samples. "M" represents the *Salmonella* H9812 DNA size marker; lanes 1–7 represent the sputum samples isolated from seven cases (new cases + pre-existing cases); and lanes 8–12 represent the environmental samples.

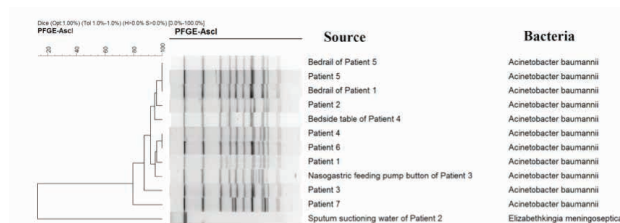


Figure 2: Analysis using the BioNumerics (version 6.5) software for the samples from seven patient cases and five environmental samples

the hospital conducted environment surface sampling in the ICU on January 30, 2015. A total of 32 samples were collected, and the bacterial growth detected was at an allowable level. The ICU was monitored between Jan. 17 to June 30, 2015, and in total nine PDR-Ab cases were detected in this 5-month period compared with the previous 13 cases from Oct. 1, 2014 to Jan. 16, 2015 (3.5 months) before launching the control measures. The number of patients decreased significantly following the implementation of prevention and control measures, and the resistance changed from PDR to MDR.

4 Discussion

Outbreaks of nosocomial infections are characterized by the occurrence of more than three cases of infection among the patients in one medical institution or department, with the infection being caused by homologous strains of the same species of pathogen within a short period of time [10]. Homology analysis was performed on the microbiological samples collected from three newly diagnosed patients (new cases) and four patients who were admitted earlier but remained in the ICU for treatment. According to the analysis results, only two cases with nosocomial infections caused by homologous strains of the same species were found. Although it was not considered to be an outbreak of nosocomial infection, the epidemiological analysis demonstrated that the rate of PDR-Ab nosocomial infection between Oct. 1, 2014 and Jan. 16, 2015 was significantly higher than the rate during the corresponding period one year prior, confirming the disease cluster.

According to our investigation, we found that the “attention unit” showed a high correlation with PDR-Ab infection. The patients in the “attention unit” were the most critical in the ICU, and their underlying diseases were serious and complex. Additionally, intubation (endotracheal intubation, central venous catheterization, and urinary catheterization), sputum suctioning, dressing changes and other procedures were frequently performed. The use of instruments such as respirators, intravenous infusion pumps and blood filtration machines were also common. The patients experienced long hospital stays and could not be transferred or discharged. Consequently, the risk of spreading a MDR infection was higher than in other units. The attention unit was considered the source of nosocomial infection for this cluster.

The results of the PFGE homology test [11, 12] indicated that the samples isolated from the bed rails of two PDR-Ab-positive patients, whose beds were adjacent, were

homologous. It is possible that environmental disinfection was not completed due to the ineffective implementation of hand hygiene guidelines among the staff, leading to the spread of pathogens through contact near the beds. In addition, PDR-Ab was also detected in the samples isolated from the instrument buttons and bedside tables, indicating that PDR-Ab survived on various surfaces that were not fully disinfected. This may have been an important contributing factor to the spread of these nosocomial infections.

In the case of a suspected outbreak of nosocomial infection, the management should pay sufficient attention and rapidly instigate appropriate emergency response plans to ensure prompt implementation of control measures according to the preliminary results of risk factor analysis. After identification of positive cases, the microbiology department should notify the clinical departments and the infection control department as soon as possible, while increasing real-time monitoring using infection surveillance software. This would increase the chances of early identification of patients infected with MDR bacteria and allow for the rapid implementation of corresponding control measures in clinical practice, thus reducing the spread of resistant bacteria. The focus of our future work will be to enhance the screening protocols for suspected outbreaks of the same bacterial species in the same ward.

It is imperative that hospitals implement strict quarantine, isolation, and environmental cleaning and disinfection policies. Healthcare staff and housekeeping workers should concentrate on hand hygiene before and after patient contact and select the correct hand washing or hand disinfection procedures. Timely isolation of patients in a single room or centralized treatment area, and the implementation of environmental cleaning and disinfection policies are crucial for reducing the spread of MDR bacterium.

In addition, the therapeutic drugs administered to patients infected with PDR-Ab were reviewed. The results revealed prolonged antibiotic courses, poly-drug regimes, and the frequent use of special and restricted antibiotics. Antibacterial drugs, especially long-term combined use of carbapenems, can easily damage the normal flora of the body, induce gene mutations in resistant strains and increase the production of endogenous resistant bacteria, such as PDR-Ab. Strict antimicrobial management should be carried out based on policies for the use of antimicrobial agents, and the capacity to treat MDR bacteria should be improved. ICU discharge management should be enhanced to reduce the length of stay for patients with chronic diseases and achieve timely transfer and dis-

charge. This may reduce the incidence of MDR infections, reduce the time of exposure to the source of infection and would have a positive effect on the prevention and control of MDR organisms.

Limitations. There may be more risk factors associated with outbreaks of PDR-Ab infection than those identified in this study. Here, only a few risk factors were tested and explored due to the limitations of the data, and the control measures were designed according to the risk factors identified. Future studies should involve a more comprehensive analysis of risk factors.

Conclusion. In this suspected nosocomial outbreak of PDR-Ab infection, a decrease in the number of infections was observed after multiple intervention and control measures were implemented. Hospitals must ensure that sufficient attention is paid towards monitoring MDR patients. The implementation of strict control measures, such as the isolation of patients, hand hygiene and environment disinfection, are crucial for reducing the spread of MDR/PDR organisms. Homologous detection is considered the “gold standard” to determine the source of infection for clusters of patients infected with pathogenic bacteria and guides the development of prevention and control measures.

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Conflict of interest statement: Authors state no conflict of interest

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