Original Article

Risk factors of multidrug-resistant Acinetobacter baumannii recurrence after successful eradication in ventilated patients

Chiung-Yu Lin a, Yu-Mu Chen a, Meng-Chih Lin a, Yu-Ping Chang a, Tung-Ying Chao a, Chin-Chou Wang a, Yuh-Chyn Tsai b, Lien Shi Shen b, Chin-Ling Li b, An-Shen Lin a, *

a Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Kaohsiung, Taiwan
b Department of Respiratory Therapy, Kaohsiung Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Kaohsiung, Taiwan

ARTICLE INFO

Article history:
Received 19 February 2015
Accepted 29 July 2015
Available online 10 June 2016

Keywords:
Multidrug-resistant Acinetobacter baumannii
Chronic respiratory failure
Risk factor
Recurrence

ABSTRACT

Background: Clinically, multidrug-resistant Acinetobacter baumannii (MDR-AB) recurrence is found in some patients although identified as successfully eradicated. We aim to discover the characteristics of patients with MDR-AB recurrence in the respiratory tract.

Methods: We retrospectively collected 106 chronic respiratory failure patients with MDR-AB harvest in pulmonary secretion culture.

Results: MDR-AB was successfully eradicated in 69 patients. Diabetes mellitus (p = 0.030, odds ratio [OR]: 2.7, 95% confidence interval [CI]: 1.1–6.4) and acute respiratory distress syndrome (p = 0.001, OR = 4.8, 95% CI: 1.8–12.7) reduce the MDR-AB eradication rate. Besides, a classification of colonization or infection was made beyond the 69 MDR-AB eradicated patients. In the colonization group, diabetes mellitus (p = 0.009; OR = 5.1, 95% CI: 1.5–17.6) is the only independent factor to increase the recurrence rate. Glycated hemoglobin level is also analyzed for each group to investigate diabetes control effect, but no significant difference found.

Conclusions: Diabetes mellitus is a risk factor of MDR-AB recurrence among MDR-AB-colonized patients; the impact of localized pneumonia patch in MDR-AB-infected patients requires further study to be clarified.

* Corresponding author. Pulmonary and Critical Care Medicine, Kaohsiung Chang Gung Memorial Hospital, 123, Dapi Rd., Niaosong Dist., Kaohsiung 833, Taiwan. Tel.: +886 7 7317123 ext. 8199; fax: +886 7 7322402.
E-mail address: anshen@adm.cgmh.org.tw (A.-S. Lin).

Peer review under responsibility of Chang Gung University.
http://dx.doi.org/10.1016/j.bj.2015.07.001
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Multidrug-resistant A. baumannii (MDR-AB) emerges as a cause of numerous global outbreaks via its strong adaptation [1–3], and it admittedly causes a considerable medical waste in most medical centers. The mechanisms of drug resistance acquisition in A. baumannii include obtaining mobile genetic elements, such as plasmids, transposons, or integrons from the surrounding [4–7]. Series of literatures contribute to the microbial agent selection against MDR-AB, including inhaled or intravenous colistin methanesulfonate, Sulbactam, or tigecycline [8–11]; However, few articles trace the disease after cured.

In clinical practice, recurrent MDR-AB respiratory tract acquisition is found in some cases although they are declared MDR-AB is successfully eradicated. The recurrent isolates easily cause an outbreak and threaten the critically ill hospitalized patients if not detected [12]. We suppose the risk factors of MDR-AB recurrence exist, and recognizing these risk factors is a benefit in clarifying the patients prone to MDR-AB recurrence. A new disease control policy may be established to detect early and control the recurrent MDR-AB. The purpose of this study is to discover the risk factors of pulmonary MDR-AB recurrence in chronic respiratory failure patients after successful eradication.

Methods

Setting and study population

Kaohsiung Chang Gung Memorial Hospital is a 2500-bed Teaching Medical Center in Southern Taiwan, and the Respiratory Care Center (RCC) is a stepwise weaning unit accumulating patients under ventilator dependence more than 21 days. Most of the patients come from internal medical, cardiologic, surgical, or neurological intensive care units. One who fails to wean his ventilator in 42 days after admitted to RCC will be transferred to out-hospital chronic facilities, or our ordinary wards, or even back to intensive care unit. The transferring indication is based on patients' medical condition.

The patients in the RCC in Kaohsiung Chang Gung Memorial Hospital between June 1, 2009, and December 31, 2011, were enrolled. As we know, there are some MDR-AB outbreaks in the period. The laboratory profile is more complete in the period as well. The inclusion criteria include age over 18 years old and harvested with MDR-AB in pulmonary secretions culture between June 1, 2009, and December 31, 2011. The exclusion criteria were patients without tracheal intubation or tracheostomy, without antibiotics therapy, with MDR-AB bacteremia or wound infection (either surgical or nonsurgical), and prior MDR-AB acquisition before the data collection.

Definition

MDR-AB is defined to be insusceptible to all of the following classes of antimicrobials: Aminoglycosides, antipseudomonal carbapenems, antipseudomonal fluoroquinolones, antipseudomonal penicillins, carbapenems, monobactams, quinolones, aminoglycosides, tetracycline, or trimethoprim/sulfamethoxazole [13,14]. Acute respiratory distress syndrome (ARDS) is defined as arterial oxygen tension to fraction of inspired oxygen ratio less than 200 [15].

The term “chronic respiratory failure” is defined as ventilator use more than 21 days, and the term “successful eradication” complies with our hospital's disease control and prevention policy that two sets of pulmonary secretion specimens in a row yield no MDR-AB in culture examinations. All the specimens should be specified for “MDR-AB detection”, and the secretion quality should be approved by our laboratory inspector. Unqualified specimens, e.g., saliva-contaminated, are not counted. Once the MDR-AB is not eradicated in 4 weeks after antibiotics initiation, the treatment fails.

If the patients received aerosolized colistin therapy only, we sorted these patients into “colonization group”. On the other hand, people are identified as “infection group” if they received any kinds of intravenous anti-MDR-AB antibiotics. This classification matches with the conventional management for MDR-AB pulmonary acquisition in our hospital. The patient's sputum culture is traced for 1 month after successful eradication. If one or more sets of sputum culture harvesting MDR-AB during the first 1 month, we define that MDR-AB recurs.

Study design

We recorded each patient’s MDR-AB culture harvesting date, antibiotics initiation date, MDR-AB successful eradication date, MDR-AB recurrence date, and antibiotics duration; meanwhile, the interval between MDR-AB cultures harvesting date to the antibiotics initiation date is calculated.

We also collected the patients’ basic information (age, gender, cigarette smoking history, and alcohol drinking history), comorbidities (diabetes mellitis, hypertension, coronary artery disease, chronic kidney disease (CKD), liver cirrhosis, chronic obstructive pulmonary disease, cerebral vascular accident, and cancer history), clinical features (ear temperature, pulse rate, respiration rate, blood pressure, fraction of inspiration oxygen, and ventilator days prior to MDR-AB treatment), and laboratory exam data (hemogram, blood gas analysis profiles, C-reactive protein, blood creatine level, sodium, and potassium). In addition, patients’ disease severity was measured in Acute...
Physiology and Chronic Health Evaluation scoring system (APACHE II) [16].

Initially, we compared the variables to look for the factors affecting MDR-AB eradication. A categorization was made on the MDR-AB-eradicated patients into colonization groups and infection groups. The variables were then analyzed to discover the risk factors of MDR-AB recurrence in each group (overall, colonization, and infection group).

The sputum culture examination after MDR-AB eradication is not a routine check-up, and we re-examine the sputum if any sign of airway infection (e.g., fever, radiologic patch, or purulent sputum). Our RCC patients may be transferred to respiratory care wards, kinds of chronic facilities adopting long-term ventilated patients, if they fail to wean the ventilators. For these patients, we can obtain their sputum specimen if they are brought back to our emergency depart to treat upper airway infection.

Owing to the finding of the diabetes’s influence to MDR-AB recurrence, a secondary investigation of diabetes control is performed via analyzing glycated hemoglobin (HbA1c) level on each group. We calculated the HbA1c receiver operating characteristic (ROC) curve to find the cut-off point, and then a comparison between better sugar control and worsen control was made.

**Statistical analysis**

Variables were analyzed with Chi-square test, Fisher’s exact test, Student’s t-test, or the Mann–Whitney U-test. Continuous, normally distributed variables were presented as mean (standard deviation), whereas non-normally distributed variables were presented as median (interquartile range). Variables with \( p < 0.05 \) in univariate analysis were included into a multivariate logistic regression.

**Ethics**

This is a retrospective study, and the study protocol was approved by the Chang Gung Medical Foundation Institutional Review Board (Project No. 103-4706B).

**Results**

From June 1, 2009, to December 31, 2011, we enrolled 295 patients with MDR-AB harvest in pulmonary secretion culture examination. After filtered with exclusion criteria, 106 patients remained and 69 (65.1%) among these patients were MDR-AB successfully eradicated [Fig. 1]. Of the variables compared, diabetes mellitus (51% vs. 30.4%, \( p = 0.034 \)) and ARDS (43.2% vs. 14.5%, \( p = 0.001 \)) are the two factors to reduce the MDR-AB eradication rate. The \( p \)-values of both variables in multivariable analysis are \(<0.05\) (diabetes: OR: 2.7, 95% CI: 1.1–6.4; ARDS OR: 4.8, 95% CI: 1.8–12.7) [Table 1]. There is no significant difference in APACHE II scores between the treatment failure group and the successful eradication group.

MDR-AB recurred in 18 (26.1%) patients after 1 month [Table 2]; we analyzed the MDR-AB recurrence risk factors in 3 groups (overall patient group, MDR-AB colonization group, and MDR-AB infection group). For the overall MDR-AB
eradicated patients, diabetes mellitus (21.6% vs. 55.6%, \( p = 0.009 \), OR [95% CI]: 5.1 [1.5–17.6]) and localized pneumonia patch (51.0% vs. 88.9%, \( p = 0.012 \), OR [95% CI]: 8.2 [1.6–42.2]) were the two recurrence risk factors. Among the colonization group, diabetes (14.3% vs. 50.0%, \( p = 0.017 \)) and ARDS (5.7% vs. 30.0%, \( p = 0.031 \)) show a significant difference in univariate analysis [Table 3]. Both diabetes and ARDS were included into a multivariate logistic regression, and the multivariate p-value [Table 3] show a significant difference in univariate analysis [Table 3]. Both diabetes and ARDS were included into a multivariate logistic regression, and the multivariate p-value [Table 3] show a significant difference in univariate analysis [Table 3].

A secondary investigation of HbA1c is performed in each study group. A total of 29 and 16 pieces of HbA1c data are obtained in the raw eligible patients (diabetes number: 40) and successful eradication patients (diabetes number: 21). The HbA1c ROC curve is analyzed in both the overall group and the MDR-AB colonization group. Of the overall group, the cut-off point is 7.0 and the area under the curve (AUC) is 0.73. Nevertheless, HbA1c < 7.0 (n = 7) and HbA1c > 7.0 (n = 9) make no significant differences in respect to MDR-AB recurrence (25.0% vs. 62.5%, \( p = 0.315 \)). There are only seven piece of data obtained in the colonization group; more case numbers are required for further analysis in this sub-group. The information of antibiotics selection in each group is provided in Table 4.

Discussion

Acinetobacter baumannii is a Gram-negative coccobacillus and tolerates long periods in both moist and dry conditions [2,3], and the easy acquisition of drug resistance makes it a great challenge in disease control. A. baumannii has become a leading cause of nosocomial pneumonia and bacteremia globally [17,18]; Nevertheless, some people doubt its clinical influence on morbidity and mortality. Recent studies began to associate A. baumannii to increased mortality and prolonged intensive care unit days [19,20]. Falagas et al. conducted a nine-study systematic review and demonstrate the relationship between A. baumannii and increased mortality [21]. He advocates that clinicians should make every effort to combat them. In fact, physicians have invested much investigation in A. baumannii opposition, including antimicrobial agent selection and anti-infection measures such as contact precautions, meticulous environmental decontamination, hand washing, or even chlorhexidine baths [8–12,22,23]. MDR-AB sometimes recurs in respiratory tract even after successful eradication, and the

### Table 1 – Baseline factors to eradicate multidrug-resistant Acinetobacter baumannii.

| Variables                          | Without eradication (n = 37) | Eradication (n = 69) | Univariate analysis P | Multivariate analysis P | OR (95% CI) |
|------------------------------------|-----------------------------|----------------------|-----------------------|-------------------------|------------|
| Age, mean (SD)                     | 76.0 (10.9)                 | 71.4 (14.0)          | 0.085                 |                         |            |
| Gender (male), n (%)               | 21 (56.8)                   | 40 (58.0)            | 0.904                 |                         |            |
| APACHE II, median (IQR)a           | 20 (18.5–21)                | 20 (17–23)           | 0.839                 |                         |            |
| Comorbidities                      |                             |                      |                       |                         |            |
| Diabetes, n (%)                    | 19 (51.4)                   | 21 (30.4)            | 0.034                 | 0.030                   | 2.7 (1.1–6.4) |
| Hypertension, n (%)                | 22 (59.5)                   | 42 (60.9)            | 0.887                 |                         |            |
| Coronary artery disease, n (%)     | 6 (16.2)                    | 15 (21.7)            | 0.496                 |                         |            |
| Chronic kidney disease, n (%)      | 6 (16.2)                    | 14 (20.3)            | 0.609                 |                         |            |
| Liver cirrhosis, n (%)             | 3 (8.1)                     | 1 (1.4)              | 0.121                 |                         |            |
| COPD, n (%)                        | 8 (21.6)                    | 12 (17.4)            | 0.596                 |                         |            |
| Cerebral vascular accident, n (%)  | 7 (18.9)                    | 21 (30.4)            | 0.200                 |                         |            |
| Cancer, n (%)                      | 5 (13.5)                    | 14 (20.3)            | 0.386                 |                         |            |
| Past histories                     |                             |                      |                       |                         |            |
| Cigarette smoking, n (%)           | 6 (16.2)                    | 12 (17.4)            | 0.878                 |                         |            |
| Alcohol drinking, n (%)            | 3 (8.1)                     | 6 (8.7)              | 1.000                 |                         |            |
| Pulmonary TB history, n (%)        | 2 (5.4)                     | 6 (8.7)              | 0.710                 |                         |            |
| Laboratory profiles               |                             |                      |                       |                         |            |
| WBC, median (IQR)                  | 11,300 (9,150–17,400)       | 11,200 (8,500–14,750) | 0.327                 |                         |            |
| Hematocrit, mean (SD)              | 31.0 (4.6)                  | 30.4 (4.7)           | 0.537                 |                         |            |
| Creatine, median (IQR)             | 0.77 (0.60–2.09)            | 0.86 (0.55–2.12)     | 0.866                 |                         |            |
| C-reactive protein, median (IQR)   | 59.6 (25.0–88.2)            | 60.1 (34.0–141.2)    | 0.276                 |                         |            |
| Clinical profiles                  |                             |                      |                       |                         |            |
| Blood pH, mean (SD)                | 7.44 (0.07)                 | 7.44 (0.07)          | 0.940                 |                         |            |
| FiO2 (%), median (IQR)             | 40.35–40                    | 40.325–40            | 0.308                 |                         |            |
| PaO2/FiO2 < 200, n (%)             | 16 (43.2)                   | 10 (41.5)            | 0.001                 | 0.001                   | 4.8 (1.8–12.7) |
| Glasgow Coma Scale, median (IQR)   | 10 (3–11)                   | 9.5 (3–11)           | 0.537                 |                         |            |
| Shock, n (%)                       | 12 (32.4)                   | 13 (18.8)            | 0.116                 |                         |            |
| Radiology                          |                             |                      |                       |                         |            |
| Localized patch, n (%)b            | 26 (70.3)                   | 41 (59.4)            | 0.270                 |                         |            |

Abbreviations: SD: Standard deviation, IQR: Interquartile range; APACHE II: Acute Physiology and Chronic Health Evaluation scoring system; COPD: Chronic obstructive pulmonary disease; TB: Tuberculosis; WBC: White blood cell; OR: Odds ratio; CI: Confidence interval; FiO2: Fraction of inspired oxygen.

a APACHE II score was measured on days of first pulmonary sputum collection.

b The radiologic character of localized patch is determined by at least one licensed chest or radiology doctor.
Table 2 – Recurrence for the overall MDR-AB-eradicated patients.

| Variables                        | Without recurrence (n = 51) | Recurrence (n = 18) | Univariate analysis P | Multivariate analysis P | OR (95% CI) |
|---------------------------------|-----------------------------|---------------------|-----------------------|-------------------------|-------------|
| Age, mean (SD)                  | 70.7 (15.1)                 | 73.7 (10.1)         | 0.603                 |                         |             |
| Gender (male), n (%)            | 31 (60.8)                   | 9 (50.0)            | 0.426                 |                         |             |
| APACHE II, median (IQR)         | 20 (16–23)                  | 21 (18–24)          | 0.195                 |                         |             |
| Chronic comorbidities           |                             |                     |                       |                         |             |
| Diabetes, n (%)                 | 11 (21.6)                   | 10 (55.6)           | 0.007                 | 0.009                   | 5.1 (1.5–17.6) |
| Hypertension, n (%)             | 29 (56.9)                   | 13 (72.2)           | 0.251                 |                         |             |
| Coronary artery disease, n (%)  | 12 (23.5)                   | 3 (16.7)            | 0.743                 |                         |             |
| Chronic kidney disease, n (%)   | 10 (19.6)                   | 4 (22.2)            | 1.000                 |                         |             |
| Liver cirrhosis, n (%)          | 0 (0.0)                     | 1 (5.6)             | 0.261                 |                         |             |
| COPD, n (%)                     | 10 (19.6)                   | 2 (11.1)            | 0.718                 |                         |             |
| Cerebral vascular accident, n (%)| 13 (25.5)                  | 8 (44.4)            | 0.133                 |                         |             |
| Cancer, n (%)                   | 11 (21.6)                   | 3 (16.7)            | 0.747                 |                         |             |
| Past histories                  |                             |                     |                       |                         |             |
| Cigarette smoking, n (%)        | 10 (19.6)                   | 2 (11.1)            | 0.718                 |                         |             |
| Alcohol drinking, n (%)         | 4 (7.8)                     | 2 (11.1)            | 0.647                 |                         |             |
| Pulmonary TB history, n (%)     | 6 (11.8)                    | 0 (0.0)             | 0.328                 |                         |             |
| Laboratory profiles             |                             |                     |                       |                         |             |
| WBC, median (IQR)               | 10,500 (8300–14,100)        | 11,650 (9000–17,050) | 0.224                 |                         |             |
| Hematocrit, mean (SD)           | 30.3 (4.7)                  | 30.8 (5.0)          | 0.703                 |                         |             |
| Creatine, median (IQR)          | 0.86 (0.59–1.82)            | 1.05 (0.46–3.60)    | 0.989                 |                         |             |
| C-reactive protein, median (IQR)| 59.5 (29.0–139.5)           | 79.9 (37.0–205.5)   | 0.557                 |                         |             |
| Clinical profiles               |                             |                     |                       |                         |             |
| Blood pH, mean (SD)             | 7.44 (0.07)                 | 7.43 (0.10)         | 0.563                 |                         |             |
| FiO2, median (IQR) (%)          | 35 (35–40)                  | 40 (35–40)          | 0.554                 |                         |             |
| PaO2/FiO2, < 200, n (%)          | 5 (11.1)                    | 5 (20.8)            | 0.113                 |                         |             |
| Glasgow Coma Scale, median (IQR)| 10 (7–10)                   | 9.5 (7.5–11)        | 0.631                 |                         |             |
| Shock, n (%)                    | 10 (20.0)                   | 3 (16.7)            | 0.784                 |                         |             |
| Radiologic characteristics      |                             |                     |                       |                         |             |
| Localized patch, n (%)          | 26 (51.0)                   | 16 (88.9)           | 0.005                 | 0.012                   | 8.2 (1.6–42.2) |
| Treatment                        |                             |                     |                       |                         |             |
| Days from culture positive to   | 3 (2–6)                     | 3 (3–4)             | 0.743                 |                         |             |
| antibiotics initiation, median (IQR)| 11 (9–14)         | 9.5 (6.75–19)       | 0.929                 |                         |             |

Abbreviations: MDR-AB: Multidrug-resistant Acinetobacter baumannii; SD: Standard deviation; IQR: Interquartile range; APACHE II: Acute Physiology and Chronic Health Evaluation scoring system; COPD: Chronic obstructive pulmonary disease; TB: Tuberculosis; WBC: White blood cell; FiO2: Fraction of inspired oxygen; OR: Odds ratio; CI: Confidence interval.

recurrent isolates being a great burden on disease control since they easily cause cross-contamination before detected.

This article investigated the risk factors of MDR-AB recurrence. We excluded patients without tracheal intubation or tracheostomy to make sure the entire specimens were collected from pulmonary secretion rather than saliva, and thus increasing the reliability of the microbial culture examination result. People with MDR-AB bacteremia or wound infection are excluded to confirm the recurrent MDR-AB isolates not related to systemic spreading. Although 65.1% people are MDR-AB eradicated, 26.1% develop MDR-AB re-acquisition after 1 month.

In addition, diabetes mellitus and ARDS are the two factors reducing MDR-AB eradication rate in our study. ARDS can be interpreted to be a more severe infectious status, and it is reasonable to have a lower cure rate. As regard to diabetes, we interestingly found that diabetes is a risk factor of treatment failure as well to the MDR-AB recurrence (either the overall patient group or the MDR-AB colonization group). Our hypothesis is that diabetes mellitus interferes with our immune system and raise difficulties in pathogen eradication. Previous studies have discovered the dysfunctions of diabetic polymorphonuclear cells and diabetic monocytes/macrophages in chemotaxis, phagocytosis, and killing [24]. The declined A. baumannii population after antimicrobial agent therapy may not be totally eliminated but causing false-positive result in eradication. The residual MDR-AB pathogen re-grows after antibiotic treatment suspension. A multicenter case-control study in Korea shows that diabetes mellitus is independently associated with hospital-acquired pneumonia caused by carbapenem-resistant Gram-negative bacteria. In this study, A. baumannii is the major pathogens of hospital-acquired pneumonia and accounted for 72.1% of the total carbapenem-resistant Gram-negative bacteria isolates [25]. This Korea study may drop a hint of a possible relation between diabetes and higher MDR-AB pneumonia incidence. Nevertheless, the influence of diabetes vanishes (17.1% vs. 62.6%, p = 0.235) when we focus on the MDR-AB infection group. Our explanation is that people in the infection group received intravenous anti-MDR-AB agents rather than aerosolized colistin only; the antibiotics selection may somehow affect the clearance of MDR-AB. The higher clear effect may lower the residual MDR-AB and overshadow the diabetes influence.

Localized pneumonia patch in the chest plain film is another risk factor of MDR-AB recurrence in the overall...
Table 3 — MDR-AB recurrence for colonization group and infection group.

| Variables                        | Without recurrence (n = 35, 16) | Recurrence (n = 10, 8) | Univariate analysis P | Multivariate analysis P | OR (95% CI) |
|----------------------------------|---------------------------------|------------------------|-----------------------|-------------------------|-------------|
| **Age, mean (SD)**               |                                 |                        |                       |                         |             |
| Colonization                     | 72.0 (13.7)                     | 72.4 (10.7)            | 0.932                 |                         |             |
| Infection                        | 67.7 (17.9)                     | 75.3 (9.8)             | 0.279                 |                         |             |
| **Gender (male), n (%)**         |                                 |                        |                       |                         |             |
| Colonization                     | 22 (62.9)                       | 7 (70.0)               | 0.677                 |                         |             |
| Infection                        | 9 (56.3)                        | 2 (25.0)               | 0.156                 |                         |             |
| **APACHE II, median (IQR)**      |                                 |                        |                       |                         |             |
| Colonization                     | 20 (15–23)                      | 19.5 (18–22)           | 0.935                 |                         |             |
| Infection                        | 20 (17–23)                      | 23 (20–24)             | 0.140                 |                         |             |
| **Chronic comorbidities**        |                                 |                        |                       |                         |             |
| Diabetes, n (%)                  |                                 |                        |                       |                         |             |
| Colonization                     | 5 (14.3)                        | 5 (50.0)               | 0.017                 | 0.039                   | 5.6 (1.09–29.03) |
| Infection                        | 6 (17.1)                        | 5 (62.6)               | 0.235                 |                         |             |
| Hypertension, n (%)              |                                 |                        |                       |                         |             |
| Colonization                     | 20 (57.1)                       | 5 (50.0)               | 0.688                 |                         |             |
| Infection                        | 9 (25.7)                        | 8 (100.0)              | 0.054                 |                         |             |
| Coronary artery disease, n (%)   |                                 |                        |                       |                         |             |
| Colonization                     | 7 (20.0)                        | 2 (20.0)               | 1.000                 |                         |             |
| Infection                        | 5 (14.3)                        | 1 (12.5)               | 0.319                 |                         |             |
| Chronic kidney disease, n (%)    |                                 |                        |                       |                         |             |
| Colonization                     | 9 (25.7)                        | 1 (10.0)               | 0.292                 |                         |             |
| Infection                        | 1 (2.9)                         | 3 (37.5)               | 0.091                 |                         |             |
| Liver cirrhosis, n (%)           |                                 |                        |                       |                         |             |
| Colonization                     | 0 (0.0)                         | 0 (0.0)                | –                     |                         |             |
| Infection                        | 0 (0.0)                         | 1 (12.5)               | 0.333                 |                         |             |
| COPD, n (%)                      |                                 |                        |                       |                         |             |
| Colonization                     | 6 (17.1)                        | 2 (20.0)               | 0.835                 |                         |             |
| Infection                        | 4 (11.4)                        | 0 (0.0)                | 0.171                 |                         |             |
| Cerebral vascular accident, n (%)|                                 |                        |                       |                         |             |
| Colonization                     | 11 (31.4)                       | 5 (50.0)               | 0.279                 |                         |             |
| Infection                        | 2 (5.7)                         | 3 (37.5)               | 0.186                 |                         |             |
| Cancer, n (%)                    |                                 |                        |                       |                         |             |
| Colonization                     | 9 (25.7)                        | 2 (20.0)               | 0.711                 |                         |             |
| Infection                        | 2 (5.7)                         | 1 (12.5)               | 0.751                 |                         |             |
| **Past histories**               |                                 |                        |                       |                         |             |
| Cigarette smoking, n (%)         |                                 |                        |                       |                         |             |
| Colonization                     | 9 (25.7)                        | 2 (20.0)               | 0.711                 |                         |             |
| Infection                        | 1 (2.9)                         | 0 (0.0)                | 0.667                 |                         |             |
| Alcohol drinking, n (%)          |                                 |                        |                       |                         |             |
| Colonization                     | 4 (11.4)                        | 2 (20.0)               | 0.402                 |                         |             |
| Infection                        | 0 (0.0)                         | 0 (0.0)                | –                     |                         |             |
| Pulmonary TB history, n (%)      |                                 |                        |                       |                         |             |
| Colonization                     | 5 (14.3)                        | 0 (0.0)                | 0.328                 |                         |             |
| Infection                        | 1 (2.9)                         | 0 (0.0)                | 0.667                 |                         |             |
| **Laboratory profiles**          |                                 |                        |                       |                         |             |
| WBC, median (IQR)                |                                 |                        |                       |                         |             |
| Colonization                     | 10,500 (6875–12,675)            | 11,400 (8075–17,050)   | 0.662                 |                         |             |
| Infection                        | 10,100 (8600–15,600)            | 12,350 (9750–19,700)   | 0.133                 |                         |             |
| Hematocrit, mean (SD)            |                                 |                        |                       |                         |             |
| Colonization                     | 30.3 (4.5)                      | 30.7 (5.1)             | 0.764                 |                         |             |
| Infection                        | 30.3 (5.2)                      | 30.9 (5.2)             | 0.796                 |                         |             |
| Creatinine, median (IQR)         |                                 |                        |                       |                         |             |
| Colonization                     | 0.86 (0.60–1.82)                | 0.82 (0.46–2.73)       | 0.754                 |                         |             |
| Infection                        | 0.81 (0.56–1.81)                | 1.60 (0.35–4.08)       | 0.830                 |                         |             |
| C-reactive protein, median (IQR) |                                 |                        |                       |                         |             |
| Colonization                     | 67.0 (23.0–139.5)               | 44.6 (29.1–104.7)      | 0.548                 |                         |             |
| Infection                        | 54.1 (37.4–148.4)               | 153.1 (56.8–222.0)     | 0.159                 |                         |             |
| **Clinical profiles**            |                                 |                        |                       |                         |             |
| Blood pH, mean (SD)              |                                 |                        |                       |                         |             |
| Colonization                     | 7.44 (0.06)                     | 7.45 (0.12)            | 0.118                 |                         |             |
| Infection                        | 7.44 (0.07)                     | 7.39 (0.07)            | 0.118                 |                         |             |

(continued on next page)
comparing with ARDS. In fact, the relationship has been
widely discussed; some people believe the intersection of
comparing diabetes and ARDS. A certain relationship between diabetes and ARDS may account for the result, and diabetes is the dominate factor while only independent risk factor after multivariate analysis. A different in univariate analysis in the “colonization group” for MDR-AB recurrence, but diabetes mellitus becomes the only independent risk factor after multivariate analysis. A certain relationship between diabetes and ARDS may account for the result, and diabetes is the dominate factor while comparing with ARDS. In fact, the relationship has been widely discussed; some people believe the intersection of hyperglycemia, metabolic abnormalities, inflammation, or therapeutic agents contributing to the relationship [26].

Owing to the finding of diabetes influence on MDR-AB eradication and recurrence, we tried to discover the relationship between MDR-AB eradication and sugar control. HbA1c was chosen as the standard to characterize sugar control, because we think HbA1c is objective and quantitative. The ROC curve made a cut-point of HbA1c > 7.0 and HbA1c > 7.0. We did not disclaim the importance of diabetes control; on the other hand, more case numbers are required to confirm its influence. Another possible explanation is that HbA1c can only represent the sugar control in the past 3 months rather than the “current sugar control status” during antimicrobial therapy. However, it is difficult to characterize current sugar control status; it is also greatly affected by the operator of the

### Table 3 – (continued)

| Variables                        | Without recurrence (n = 35, 16) | Recurrence (n = 10, 8) | Univariate analysis P | Multivariate analysis P | OR (95% CI)d |
|----------------------------------|--------------------------------|------------------------|------------------------|-------------------------|--------------|
| FiO₂ (%), median (IQR)           |                                |                        |                        |                         |              |
| Colonization                     | 35 (30–40)                     | 40 (35–40)             | 0.261                  |                         |              |
| Infection                        | 35 (37.5–40)                   | 40 (32.5–47.5)         | 0.551                  |                         |              |
| PaO₂/FiO₂ < 200, n (%)           |                                |                        |                        |                         |              |
| Colonization                     | 2 (5.7)                        | 3 (30.0)               | 0.031                  |                         |              |
| Infection                        | 3 (8.6)                        | 2 (25.0)               | 0.593                  |                         |              |
| Glasgow Coma Scale, median (IQR) |                                |                        |                        |                         |              |
| Colonization                     | 10 (7–11)                      | 7.25 (8.5–10.25)       | 0.631                  |                         |              |
| Infection                        | 8.5 (7–10)                     | 11 (6.75–11)           | 0.188                  |                         |              |
| Shock, n (%)                     |                                |                        |                        |                         |              |
| Colonization                     | 8 (22.9)                       | 2 (20.0)               | 0.848                  |                         |              |
| Infection                        | 2 (5.7)                        | 1 (12.5)               | 0.751                  |                         |              |
| Radiologic characteristics       |                                |                        |                        |                         |              |
| Localized patch, n (%)           |                                |                        |                        |                         |              |
| Colonization                     | 18 (51.4)                      | 8 (80.0)               | 0.297                  |                         |              |
| Infection                        | 8 (50)                         | 8 (100)                | 0.022c                 |                         |              |
| Treatment                        |                                |                        |                        |                         |              |
| Days from culture positive to    |                                |                        |                        |                         |              |
| antibiotics initiation, median    |                                |                        |                        |                         |              |
| (IQR)                            |                                |                        |                        |                         |              |
| Colonization                     | 3 (2–6)                        | 3 (2–4)                | 0.429                  |                         |              |
| Infection                        | 3 (2–5)                        | 4 (3–4)                | 0.432                  |                         |              |
| Antibiotics duration, median (IQR)|                                |                        |                        |                         |              |
| Colonization                     | 11 (9–14)                      | 9.5 (6.75–11.25)       | 0.099                  |                         |              |
| Infection                        | 11 (9–20)                      | 14 (7–22)              | 0.877                  |                         |              |

Abbreviations: MDR-AB: Multidrug-resistant Acinetobacter baumannii; SD: Standard deviation; IQR: Interquartile range; APACHE II: Acute Physiology and Chronic Health Evaluation scoring system; COPD: Chronic obstructive pulmonary disease; TB: Tuberculosis; WBC: White blood cell; FiO₂: Fraction of inspired oxygen; OR: Odds ratio; CI: Confidence interval.

a The number of “colonization group” and “infection group” in without recurrence section is 35 and 16, respectively.

b The number of “colonization group” and “infection group” in recurrence section is 10 and 8, respectively.

c Localized patch is the only risk factor of recurrence in the infection group; however, there is no variation in the recurrence group. More subjects for the infection group are required to clarify this impact.

d The ORs are obtained from the univariate analysis, instead of multiple logistic regression.

### Table 4 – Comparing the initial antibiotics selection in each group.

| Variables                      | Without eradication, n (%) | Eradication, n (%) | Recurrence |
|--------------------------------|----------------------------|-------------------|------------|
| Colonization group             |                            |                   |            |
| Aerosolized colistin only (n = 64) | 19 (29.7)                  | 45 (70.3)         | 10         |
| Infection group                |                            |                   |            |
| Intravenous colistin (n = 1)   | 1 (100.0)                  | 0 (0.0)           | –          |
| Tigecycline (n = 9)            | 7 (77.8)                   | 2 (22.2)          | 1          |
| Sulbactam (n = 4)              | 0 (0.0)                    | 4 (100.0)         | 1          |
| Aerosolized colistin +        | 9 (39.1)                   | 14 (60.9)         | 6          |
| Tigecycline (n = 23)           | 4 (20.0)                   | 0 (0.0)           | 0          |
| Aerosolized colistin + sulbactam (n = 5) | 1 (20.0)                  | 4 (80.0)         | 0          |
fingertip testing (e.g., insufficiency time between the food intake and fingertip testing).

The treatment on MDR-AB-colonized patients is controversial, and some physicians even advocate that antibiotics are not necessary in colonized cases. In our experience, MDR-AB colonization makes a huge medical waste since they may cause another outbreak if the lack of strict hand washing policies. Besides these, patients are often rejected from local chronic facilities and thus seriously reduced the bed availability in medical centers. In our opinion, the importance of MDR-AB colonization in our study still provides certain use in practice if intensive MDR-AB eradication is demanded by clinical physicians.

To the best of our knowledge, our research is the first one to study the MDR-AB recurrence. A more aggressive disease control policy, prolonged duration of contact precautions, or meticulous environmental decontamination is considered on those infected by MDR-AB. Besides, we propose a higher standard eradication criteria and intensive pulmonary secretion culture check-up on these patients to prevent a possible cross-infection to other hosts.

There are limitations to this study. First, we excluded patients without antibiotics treatment in our study since they are usually identified to be MDR-AB-colonized. This group did not receive intensive pulmonary secretion culturing exam or laboratory exams and will easily cause bias. We, therefore, miss the information of MDR-AB recurrence in spontaneously MDR-AB-eradicated patients. A well-designed prospective study in the future may be required to solve the situation. Second, we do not perform molecular examination due to equipment limitation and failed to distinguish the recurrence MDR-AB from the origin strain or cross-infected strain. Last, most people enrolled in our study received aerosolized colistin rather than intravenous colistin; it is because the high proportion of old age or CKD patients in RCC. Concerning the possibility of colistin-related kidney injury [27], physicians seldom prescribe intravenous colistin unless MDR-AB bacteremia or high disease severity. However, this concept is challenged nowadays since some debate that colistin give a relatively high clinical cure rates and over-estimated in the incidence of kidney injury [28].

Conclusion

Diabetes mellitus and ARDS are risk factors to affect MDR-AB eradication. For the overall MDR-AB-eradicated patients, diabetes mellitus and localized pneumonia patch are the two risk factors. As regards to the MDR-AB colonization group, diabetes mellitus is the only independent factor to increase the recurrence rate. The localized patch in the infection group and the influence of HbA1c require further investigation. Recognizing the risk factors contributes to early detection of disease recurrence and preventing the possible cross-contamination to other hosts.

Source of support

Nil.

Conflicts of interest

No conflicts of interest.

Acknowledgments

All the information is gathered from Kaohsiung Chang Gung Memorial Hospital database. Each author participates sufficiently in the work to take public responsibility for each portion of the content. The contribution of each author is listed below.

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