Clinical Characteristics in Patients with Hospital-Acquired Pneumonia Caused by Extensively Drug-Resistant *Acinetobacter baumannii*, A Multicenter Retrospective Study

Yujun Li
South China University of Technology School of Medicine
Xiaomei Huang
South China University of Technology School of Medicine
Yuyao Wang
Danbury Hospital
Chuzhi Pan
al Third Affiliated Hospitof Sun Yat-Sen University
Zexun Mo
South China University of Technology School of Medicine
Muchao Huang
Guangzhou Xinhai Hospital
Changquan Fang
Guangzhou Red Cross Hospital
Penghao Guo
Sun Yat-sen University First Affiliated Hospital
Huiling Chen
South China University of Technology School of Medicine
Zhuxiang Zhao
South China University of Technology School of Medicine
Ziwen Zhao
South China University of Technology School of Medicine
Shuquan Wei (eyweishuquan@scut.edu.cn)
Guangzhou First People's Hospital https://orcid.org/0000-0003-4044-2244

Research article

Keywords: Acinetobacter baumannii, Extensive drug resistance, Pneumonia, multicenter retrospective study

Posted Date: December 1st, 2020

DOI: https://doi.org/10.21203/rs.3.rs-116166/v1

Abstract

Background Extremely drug-resistant (XDR) *Acinetobacter baumannii* (*A. baumannii*) has been of a great concern. The relationship between XDR and patient outcomes remains unclear. We investigated the clinical features, risk factors, and outcomes of Hospital-acquired pneumonia (HAP)caused by XDR *A. baumannii.*

Methods A multicenter retrospective case-control study was performed to determine factors associated with XDR *A. baumannii* pneumonia from 5 teaching hospitals in Guangzhou, China.

Results 76 patients were enrolled in the study. XDR *A. baumannii* pneumonia patients were tend to be smoker (11.9% vs 3.9%, P = 0.130) and older (76.5±11.2 vs 70.3±16.4, P = 0.007) and had more comorbid diseases including chronic obstructive pulmonary disease (COPD) (48.7% vs 21.1%, P = 0.001) and renal failure (21.1% vs 3.9%, P = 0.002) and had higher APACHE II score (65.8% vs 47.4%, P = 0.033). Invasive procedures including insertion of urinary catheter, nasogastric tube, central venous/arterial catheter, bronchoscopy and mechanical ventilation along with using β-lactam/β-lactamase inhibitor and carbapenem were also risk factors for XDR *A. baumannii* pneumonia. Multivariate analysis showed the APACHE II score >=20 (OR, 2.1; 95% CI: 1.1–4.1, P = 0.023), COPD (OR, 9.6; 95% CI: 2.0–45.5, P = 0.004), central venous/arterial catheter placement (OR,11.5; 95% CI: 1.1-117.8, P = 0.040), low albumin levels (OR, 1.2; 95% CI: 1.1-1.4, P = 0.001) and using β-lactam/β-lactamase inhibitor (OR,15.9; 95% CI: 2.7-94.2, P = 0.002) were independent risk factors for XDR *A. baumannii* pneumonia. Compared with the non-XDR *A. baumannii* patients, the XDR *A. baumannii* pneumonia increased length of mechanical ventilation (11.1±12.3 vs 5.1±5.6, P = 0.000), hospital stay (42.2±24.3 vs 34.8±18.0, P = 0.036) and ICU (Intensive Care Unit) stay (27.5±19.0 vs 20.0±20.5, P = 0.020), but it did not increase in-hospital mortality (47.4% vs 32.9%, P = 0.137).

Conclusions XDR *A. baumannii* pneumonia was strongly related to systemic illnesses, invasive procedure, low albumin levels and the APACHE II score and increasing the length of mechanical ventilation and hospital stay. But it did not increase in-hospital mortality.

Background

Acinetobacter baumannii (*A. baumannii*) is one of the most troublesome pathogens causing Hospital-acquired pneumonia (HAP) worldwide[1–3]. Due to its remarkable ability to acquire antibiotic resistance, *A. baumannii* infection is also difficult to control and treat[4–6]. CHINET surveillance system from China showed *A. baumannii* resists to many powerful antimicrobial agents, especially imipenem and meropenem which were once considered as the “gold standard”[7]. And the resistance rate to those agents went up to 77.1% and 78.1% respectively in 2018[6]. Extremely drug-resistant (XDR) *A. baumannii* was defined as resistance to all available antibiotics except for colistin and tigecycline[8–10]. It became a major resistance phenotype, ranged from 68.3–72.9% of the reported *A. baumannii* strains[11, 12]. Colistin and tigecycline are believed to be the last few available choices for XDR infections. But

tigecycline and polymyxin resistance *A. baumannii* had already been reported[5, 13–15]. XDR *A. baumannii* with limited treatment options was believed to be associated with high mortality and treatment failure and served as a marker of poor prognosis.

However, the relationship between antibiotic resistance of *A. baumannii* strains and outcomes caused with concern and dispute. One study in 2007 found mortality rates of patients with multi-drug resistant (MDR) *A. baumannii* were not higher than the patients without MDR *A. baumannii* [16]. Our previous study in 2017 was limited by the sample size, but it showed XDR *A. baumannii* pneumonia was not associated with in-hospital mortality[10]. Two studies in 2019 showed increasing mortality rate may relate to patient comorbidity and inappropriate therapy, but not antibiotic resistance [12, 17]. It is frustrated for clinicians to treat XDR *A. baumannii* and the data for XDR *A. baumannii* HAP was still limited. We believe the relationship between XDR *A. baumannii* pneumonia and outcomes needs further investigation. Here, we conducted a multicenter study to investigate the clinical features, risk factors, and outcomes of HAP caused by XDR *A. baumannii* from 5 teaching hospitals in Guangzhou, China.

Methods

Participants

A multicenter retrospective case-control study was conducted to evaluate the clinical features, risk factors, and outcomes of HAP caused by XDR *A. baumannii* from 5 teaching hospitals in Guangzhou, China. GFPH, Guangzhou First People's Hospital, the Second Affiliated Hospital of South China University of Technology, Pan Fu Road, Guangzhou, China; TAH, the Third Affiliated Hospital of Sun Yat-sen University, Tian He Road, Guangzhou, China; FAH, the First Affiliated Hospital of Sun Yat-sen University, Zhong Shan Er Road, Guangzhou, China; GXH, Guangzhou Xinhai Hospital, Xin Gang west Road, Guangzhou, China; GRCH, Guangzhou Red Cross Hospital, Tong Fu zhong Road, Guangzhou, China. The participants included patients who developed HAP and ventilator-associated pneumonia (VAP) [12] from XDR *A. baumannii* (confirmed with respiratory samples) from April 2011 to April 2016. The controls, matched to the cases by hospitals, were patients diagnosed with non-XDR *A. baumannii* HAP and randomly selected within the 5 teaching hospitals during the studying period.

Inclusion and exclusion criteria

The inclusion criteria consisted of the following:

1, Diagnostic criteria for pneumonia[18]: new or progressive pulmonary infiltrates in chest X-ray or CT imaging, plus at least two of the following supportive clinical signs: temperature of > 38 °C or < 35.5 °C, leukocytosis of > 12,000 or < 4000 WBC/mm^3, purulent respiratory secretions, or worsening oxygenation determined by arterial oxygen tension/fraction of inspired oxygen ratio (PaO_2/FiO_2).

2, At least two positive clinical respiratory cultures for *A. baumannii*: protected brushing specimen 10^3 CFU/ml, bronchoalveolar lavage (BAL) fluid specimen 10^4 or 10^5 CFU/ml, or endotracheal aspirate specimen 10^6 CFU/ml.

3, Antimicrobial susceptibility testing shows resistance to all available antibiotics except for colistin and tigecycline.

The exclusion criteria consisted of the following:

1, Patient was less than 18 years of age.

2, The length of hospitalization was less than 48 hours.

3, Patient had incomplete medical records.

4, Patient had other non- *A. baumannii* - positive respiratory cultures.

Data acquisition

A specially designed case record form (CRF) was used to collect the patient's clinical parameters, including age, gender, cigarette smoking, substance use history, laboratory test results (white blood cell count, platelet count, hemoglobin, creatinine, CRP, ESR and albumin), past medical diseases, invasive procedures (venous or arterial catheter placement, bronchoscopy, mechanical ventilation, et al.), the length of hospital stay (including ICU), pharmaceutical records (including antibiotic exposure), microbiological records (bacterial etiology, culture, and antimicrobial susceptibility testing results) and in-hospital mortality. The Acute Physiology and Chronic Health Evaluation (APACHE) II score was used to determine the severity of diseases on patient's admission. The in-hospital mortality was compared between the HAP with and without XDR *A. baumannii* infection groups. The Guangzhou First People's Hospital, the Second Affiliated Hospital of South China University of Technology Ethics Committee approved the study.

Statistical analysis

SPSS (version 18.0) was used for statistical analysis. A P value less than 0.05 was considered statistically significant. Categorical variables were compared using the Chi-square test with Yates correction or Fisher's exact test. Continuous variables were analyzed using the two-tailed t-test. A multivariate logistic regression model was used to test the independent risk factors for XDR *A. baumannii* pneumonia.

Results

Based on the inclusion and exclusion criteria, a total of 76 patients with XDR *A. baumannii* pneumonia were included in the case-control study. 53 were male and 23 were female. The mean age was 76.5-year-old with a standard deviation of 11.2 years (Table 1). To analyze the potential risk factors, 76 cases of patients were compared with 76 control patients.

Table 1
Clinical characteristics in HAP patients with XDR *A. baumannii* and non-XDR *A. baumannii*

	XDR *A. baumannii* (N = 76)	Non-XDR *A. baumannii* (N = 76)	P-value
Age, y*	76.5 ± 11.2	70.3 ± 16.4	0.007
Gender (M/F), n	53/23	48/28	0.492
Cigarette smoking, n (%)	41 (53.9)	11 (14.5)	0.000
Alcohol abuse, n (%)	9 (11.8)	3 (3.9)	0.130
APACHE II score > = 20	50 (65.8)	36 (47.4)	0.033
White blood cell count(10^9/L)*	15.8 ± 6.5	13.0 ± 5.0	0.003
Platelet count (10^9/L) *	161.4 ± 77.5	170.7 ± 86.0	0.486
Hemoglobin (g/L) *	102.5 ± 22.0	109.1 ± 23.4	0.074
Creatinine (μmol /L) *	161.9 ± 154.3	126.4 ± 109.5	0.104
CRP (g/L) *	62.6 ± 50.3	69.2 ± 58.0	0.180
ESR (MM/H) *	50.1 ± 39.8	69.2 ± 58.0	0.486
Albumin (g/L) *	29.1 ± 4.4	41.8 ± 31.5	0.002
Time related to hospitalization*			
Days of mechanical ventilation (days)	11.1 ± 12.3	5.1 ± 5.6	0.000
Length of hospital stay before HAP (days)	8.6 ± 7.5	8.8 ± 8.1	0.861
Length of stay in the ICU (days)	27.5 ± 19.0	20.0 ± 20.5	0.020
Length of stay in the hospital (days)	42.2 ± 24.3	34.8 ± 18.0	0.036
Associated disease, n (%)			
COPD	37 (48.7)	16 (21.1)	0.001
Diabetes mellitus	26 (22.4)	33 (43.4)	0.318
Malignancy	9 (11.8)	17 (22.4)	0.131
Coronary heart disease	28 (36.8)	21 (27.6)	0.298

*Values are presented as the mean ± standard deviation; COPD, Chronic obstructive pulmonary disease; Malignancy includes haematological malignancies and solid tumours; CRP, C-reactive protein; ESR, Erythrocyte sedimentation rate; PPIs, proton pump inhibitor drugs.

	XDR *A. baumannii* (N = 76)	Non-XDR *A. baumannii* (N = 76)	P-value
Renal failure	16 (21.1)	3 (3.9)	0.002
Cerebral haemorrhage	8 (10.5)	7 (9.2)	1.000
Device, n (%)			
Urinary catheter	76 (100.0)	65 (85.5)	0.001
Nasogastric tube	76 (100.0)	62 (81.6)	0.000
Central venous/arterial catheter	73 (96.1)	49 (64.5)	0.000
Bronchoscope	65 (85.5)	51 (67.1)	0.012
Mechanical ventilation	70 (92.1)	55 (72.4)	0.002
Tracheotomy	7 (9.2)	4 (5.3)	0.533
Drug usage, n (%)			
Glucocorticoids	47 (61.8)	35 (46.1)	0.073
PPIs	61 (82.9)	56 (82.9)	0.441
Antimicrobial n (%)			
Cephalosporin	37 (48.7)	42 (55.3)	0.516
Second generation	11 (14.5)	14 (18.4)	0.662
Third generation	30 (39.5)	33 (43.4)	0.742
β-lactam/β-lactamase inhibitor	71(93.4)	52 (68.4)	0.000
Quinolone	44 (57.9)	33 (43.4)	0.104
Aminoglycoside	5 (6.6)	6 (7.9)	1.000
Macrolides	2 (2.6)	0 (0.0)	0.497
Carbapenem	35 (46.1)	14(18.4)	0.000
Antimicrobial Combination therapy, n (%)	39 (51.3)	30 (39.5)	0.192
Mortality, n (%)	36 (47.4)	26(32.9)	0.137

*Values are presented as the mean ± standard deviation; COPD, Chronic obstructive pulmonary disease; Malignancy includes haematological malignancies and solid tumours; CRP, C-reactive protein; ESR, Erythrocyte sedimentation rate; PPIs, proton pump inhibitor drugs.

Table 2
Multi-variate analysis of risk factors for XDR *A. baumannii* HAP patients

Risk factor	OR (95% CI)	P-value
APACHE II score > = 20	2.1 (1.1–4.1)	0.023
COPD	9.6 (2.0-45.5)	0.004
Central venous/arterial catheter	11.5 (1.1-117.8)	0.040
Albumin	1.2 (1.1–1.4)	0.001
β-lactam/β-lactamase inhibitor	15.9 (2.7–94.2)	0.002

The two groups were similar with respect to gender, substance use history, platelet count, hemoglobin, creatinine, CRP and ESR level. Additionally, no significant differences in the length of hospital stay before developing XDR *A. baumannii* pneumonia, history of diabetes mellitus, malignancy, coronary heart disease, renal failure, cerebral haemorrhage, tracheotomy, or the use of glucocorticoids, PPIs, cephalosporin, quinolone, macrolides, minoglycoside or antimicrobial combination therapy. While compared with the non-XDR *A. baumannii* patients, the patients with XDR *A. baumannii* pneumonia were more likely in smoking (11.9% vs 3.9%, P = 0.130), older patients (76.5 ± 11.2 vs 70.3 ± 16.4, P = 0.007), APACHE II score up to 20 and higher (65.8% vs 47.4%, P = 0.033), longer length of mechanical ventilation (11.1 ± 12.3 vs 5.1 ± 5.6, P = 0.000), longer length of in hospital stay (42.2 ± 24.3 vs 34.8 ± 18.0, P = 0.036) and ICU stay (27.5 ± 19.0 vs 20.0 ± 20.5, P = 0.020), receiving more invasive procedure including insertion of urinary catheter (100.0% vs 85.5%, P = 0.001) and nasogastric tube (100.0% vs 81.6%, P = 0.000), central venous/arterial catheter placement (96.1% vs 64.5%, P = 0.000), bronchoscopy (85.5% vs 67.1%, P = 0.012) and mechanical ventilation (92.1% vs 72.4%, P = 0.002). Moreover, patients with XDR *A. baumannii* pneumonia were more likely to have more comorbid diseases, such as chronic obstructive pulmonary disease (COPD) (48.7% vs 21.1%, P = 0.001) and renal failure (21.1% vs 3.9%, P = 0.002). Using β-lactam/β-lactamase inhibitor (93.4% vs 68.4%, P = 0.001) or carbapenem (46.1% vs 18.4%, P = 0.000) was also a risk factor for XDR *A. baumannii* pneumonia. But compared with the non-XDR *A. baumannii* patients, the XDR *A. baumannii* pneumonia did not increase in-hospital mortality (47.4% vs 32.9%, P = 0.137) (Tables 1).

Multivariate analysis using a logistic regression model showed that the APACHE II score > = 20 (OR, 2.1; 95% CI: 1.1–4.1, P = 0.023), COPD (OR, 9.6; 95% CI: 2.0–45.5, P = 0.004), central venous/arterial catheter (OR,11.5; 95% CI: 1.1-117.8, P = 0.040), lower albumin levels (OR, 1.2; 95% CI: 1.1–1.4, P = 0.001) and using β-lactam/β-lactamase inhibitor (OR,15.9; 95% CI: 2.7–94.2, P = 0.002) were identified as independent risk factors for XDR *A. baumannii* pneumonia.

Discussion

XDR *A. baumannii* infection rate kept rising. But the antibiotics treatment options were very limited. It made the XDR *A. baumannii* one of the most troublesome pathogens worldwide. It seems preventing spreading the pathogen is the only reasonable way to reduce mortality. However, recently, the relationship between antibiotic resistance and outcomes caused with concern and dispute. Here, we presented this multicenter retrospective case-control study to investigate the clinical features, risk factors, and outcomes of HAP caused by XDR *A. baumannii*. It showed XDR *A. baumannii* pneumonia significantly increased the length of mechanical ventilation and hospital stay. But it was not associated with in-hospital mortality. Our finding indicated, besides antibiotics, we could improve outcomes if we optimize treatment in XDR *A. baumannii* pneumonia patients. This study may provide an insight view of XDR *A. baumannii* pneumonia clinical management during an era of stagnation in new antibiotic development.

Our study found that XDR *A. baumannii* pneumonia patients were more likely to have a smoking history and in elderly patients with complicated underlying disease and severer initial presentation (higher APACHE II score). It was similar to previous studies[19–21]. Multivariate logistic regression analysis showed the APACHE II score greater than 20, COPD, and lower albumin levels were the independent risk factors for XDR *A. baumannii* pneumonia. Those findings indicated immunocompromised patients were more likely to develop XDR *A. baumannii* HAP. Using β-lactam/β-lactamase inhibitors was also another independent risk factor. Clinicians need to be extra careful while using β-lactam/β-lactamase inhibitors. XDR *A. baumannii* pneumonia patients may receive more invasive procedures due to severer clinical presentation. But medical devices may be the most contaminated locations for *A. baumannii* and caused hospital-acquired infections outbreaks [22, 23]. Therefore, clinicians should be aware of invasive procedures uses and removing unnecessary accesses in time.

Previous studies had shown patients with antibiotic-resistant *A. baumannii* may have increased mortality compared with antibiotic-sensitive patients. [16, 24, 25]. The study in 2018 showed the increased mortality rate was associated with patient comorbidity and inappropriate therapy, but not antibiotic resistance[26]. And more studies revealed antibiotic resistance of *A. baumannii* was not associated with increase mortality. Sunenshine RH, et al[16] reported mortality rate of MDR *A. baumannii* infection patients was not higher than non-MDR *A. baumannii* patients. Özgür et al[9] also found the mortality rate of patients with XDR *A. baumannii* VAP was not significantly higher than non-XDR *A. baumannii* patients in ICU settings. Aušra C˘ iginskiene, et al[12] reported the mortality rate in XDR *A. baumannii* VAP patients was not a significant difference compared with the non-XDR group. Zilberberg et al[17] examined the impact of carbapenem-resistance (CR) in patients with HAP and VAP in a large database of 8,969 patients. In this study, *A. baumannii* accounted for 11.8% of CR organisms and 2.5% of carbapenem-susceptible (CS) organisms and did not increase mortality for CR *A. baumannii* infection (22.9% CR vs 21.6% CS). In our study, we found XDR *A. baumannii* pneumonia patients were associated with longer length of mechanical ventilation and hospital stay, but we did not observe increased in-hospital mortality. Those findings suggested resistance did not directly add to mortality and we may still improve patient outcomes if we optimize treatment with XDR *A. baumannii* pneumonia patients.

Conclusions

XDR *A. baumannii* HAP was strongly related to systemic illnesses, invasive procedures, low albumin levels, the APACHE II score, longer length of mechanical ventilation, and hospital stay. But it did not increase in-hospital mortality.

List Of Abbreviations

A. baumannii, *Acinetobacter baumannii*; GFPH, Guangzhou First People's Hospital; FAH, the First Affiliated Hospital of Sun Yat-sen University; TAH, the Third Affiliated Hospital of Sun Yat-sen University; GRCH, Guangzhou Red Cross Hospital GXH, Guangzhou Xinhai Hospital; XDR, extremely drug-resistant; HAP, hospital-acquired pneumonia; VAP, ventilator-associated pneumonia; BAL, bronchoalveolar lavage; CRF, case record form; CRP, C-reactive protein; ESR, Erythrocyte sedimentation rate; PPIs, proton pump inhibitor drugs; CR, carbapenem-resistance; CS, carbapenem-susceptible.

Declarations

Ethics approval and consent to participate

The Guangzhou First People's Hospital Ethics Committee approved the study. Informed consents were not required as this was considered a review of clinical practice.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This work was funded by the Guangzhou Medical and Health Science and Technology Project (no. 20151A011004) and Guangzhou Science and Technology Project (No. 202002030036).

Natural Science Foundation of Guangdong Province (No. 2017A030313860).

Authors' contributions

YjL supervised the study and wrote the manuscript. XmH, WyY and CzP discussed the data and helped finalize the manuscript. ZxM, ZxZ, McH, CqF, HlC and PhG collected the data. ZwZ and SqW planned and supervised the experiments. All authors read and approved the final manuscript.

Acknowledgements

We thank Yongrou Yu, Guangdong Pharmaceutical University, Guangdong, China, for helping data acquisition.

References

1. Ozyurt S, Kostakoglu U, Yildiz IE, Erturk A, Sonmez E, Sahin U, Cicek AC: **Investigation of the clonal associations in Acinetobacter Baumannii strains isolated from the respiratory samples of patients in a tertiary research hospital**. *Nigerian journal of clinical practice* 2020, **23**(8):1155-1162.
2. Boettger BC, Cayô R, Streling AP, Nodari CS, Almeida LGP, Martins W, Girardello R, Vasconcelos ATR, Gales AC, Pignatari ACC: **Dynamic of High-Risk Acinetobacter baumannii Major Clones in a Brazilian Tertiary Hospital During a Short Time Period**. *Microbial drug resistance (Larchmont, NY)* 2020.
3. Mohd Sazlly Lim S, Zainal Abidin A, Liew SM, Roberts JA, Sime FB: **The global prevalence of multidrug-resistance among Acinetobacter baumannii causing hospital-acquired and ventilator-associated pneumonia and its associated mortality: A systematic review and meta-analysis**. *The Journal of infection* 2019, **79**(6):593-600.
4. Abdallah M, Alsaleh H, Baradwan A, Alfawares R, Alobaid A, Rasheed A, Soliman I: **Intraventricular Tigecycline as a Last Resort Therapy in a Patient with Difficult-to-Treat Healthcare-Associated Acinetobacter baumannii Ventriculitis: a Case Report**. *SN comprehensive clinical medicine* 2020:1-5.
5. Nurtop E, Bayındır Bilman F, Menekse S, Kurt Azap O, Gönen M, Ergonul O, Can F: **Promoters of Colistin Resistance in Acinetobacter baumannii Infections**. *Microbial drug resistance (Larchmont, NY)* 2019, **25**(7):997-1002.
6. Hu F, Guo Y, Yang Y, Zheng Y, Wu S, Jiang X, Zhu D: **Resistance reported from China antimicrobial surveillance network (CHINET) in 2018**. 2019, **38**(12):2275-2281.
7. Garnacho-Montero J, Ortiz-Leyba C, Jiménez-Jiménez FJ, Barrero-Almodóvar AE, García-Garmendia JL, Bernabeu-Wittel IM, Gallego-Lara SL, Madrazo-Osuna J: **Treatment of multidrug-resistant Acinetobacter baumannii ventilator-associated pneumonia (VAP) with intravenous colistin: a comparison with imipenem-susceptible VAP**. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* 2003, **36**(9):1111-1118.
8. Batirel A, Balkan, Il, Karabay O, Agalar C, Akalin S, Alici O, Alp E, Altay FA, Altin N, Arslan F *et al*: **Comparison of colistin-carbapenem, colistin-sulbactam, and colistin plus other antibacterial agents for the treatment of extremely drug-resistant Acinetobacter baumannii bloodstream infections**. *European journal of clinical microbiology & infectious diseases : official publication of the European Society of Clinical Microbiology* 2014, **33**(8):1311-1322.

9. Özgür ES, Horasan ES, Karaca K, Ersöz G, Naycı Atış S, Kaya A: **Ventilator-associated pneumonia due to extensive drug-resistant Acinetobacter baumannii: risk factors, clinical features, and outcomes**. *American journal of infection control* 2014, **42**(2):206-208.
10. Li YJ, Pan CZ, Fang CQ, Zhao ZX, Chen HL, Guo PH, Zhao ZW: **Pneumonia caused by extensive drug-resistant Acinetobacter baumannii among hospitalized patients: genetic relationships, risk factors and mortality**. *BMC infectious diseases* 2017, **17**(1):371.
11. Li Y, Pan C, Zhao Z, Zhao Z, Chen H, Lu W: **Effects of a combination of amlodipine and imipenem on 42 clinical isolates of Acinetobacter baumannii obtained from a teaching hospital in Guangzhou, China**. *BMC infectious diseases* 2013, **13**:548.
12. Čiginskienė A, Dambrauskienė A, Rello J, Adukauskienė D: **Ventilator-Associated Pneumonia due to Drug-Resistant Acinetobacter baumannii: Risk Factors and Mortality Relation with Resistance Profiles, and Independent Predictors of In-Hospital Mortality**. *Medicina (Kaunas, Lithuania)* 2019, **55**(2).
13. Gerson S, Lucaßen K, Wille J, Nodari CS, Stefanik D, Nowak J, Wille T, Betts JW, Roca I, Vila J *et al*: **Diversity of amino acid substitutions in PmrCAB associated with colistin resistance in clinical isolates of Acinetobacter baumannii**. *International journal of antimicrobial agents* 2020, **55**(3):105862.
14. He T, Wang R, Liu D, Walsh TR, Zhang R, Lv Y, Ke Y, Ji Q: **Emergence of plasmid-mediated high-level tigecycline resistance genes in animals and humans**. 2019, **4**(9):1450-1456.
15. Wang L, Liu D, Lv Y, Cui L, Li Y, Li T, Song H, Hao Y, Shen J, Wang Y *et al*: **Novel Plasmid-Mediated tet(X5) Gene Conferring Resistance to Tigecycline, Eravacycline, and Omadacycline in a Clinical Acinetobacter baumannii Isolate**. *Antimicrobial agents and chemotherapy* 2019, **64**(1).
16. Sunenshine RH, Wright MO, Maragakis LL, Harris AD, Song X, Hebden J, Cosgrove SE, Anderson A, Carnell J, Jernigan DB *et al*: **Multidrug-resistant Acinetobacter infection mortality rate and length of hospitalization**. *Emerging infectious diseases* 2007, **13**(1):97-103.
17. Zilberberg MD, Nathanson BH, Sulham K, Fan W, Shorr AF: **A Novel Algorithm to Analyze Epidemiology and Outcomes of Carbapenem Resistance Among Patients With Hospital-Acquired and Ventilator-Associated Pneumonia: A Retrospective Cohort Study**. *Chest* 2019, **155**(6):1119-1130.
18. Horan TC, Andrus M, Dudeck MA: **CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting**. *American journal of infection control* 2008, **36**(5):309-332.
19. Dent LL, Marshall DR, Pratap S, Hulette RB: **Multidrug resistant Acinetobacter baumannii: a descriptive study in a city hospital**. *BMC infectious diseases* 2010, **10**:196.
20. Zheng YL, Wan YF, Zhou LY, Ye ML, Liu S, Xu CQ, He YQ, Chen JH: **Risk factors and mortality of patients with nosocomial carbapenem-resistant Acinetobacter baumannii pneumonia**. *American journal of infection control* 2013, **41**(7):e59-63.
21. Li Y, Guo Q, Wang P, Zhu D, Ye X, Wu S, Wang M: **Clonal dissemination of extensively drug-resistant Acinetobacter baumannii producing an OXA-23 β-lactamase at a teaching hospital in Shanghai,**

China. *Journal of microbiology, immunology, and infection = Wei mian yu gan ran za zhi* 2015, **48**(1):101-108.

22. Raro OHF, Gallo SW, Ferreira CAS, Oliveira SD: **Carbapenem-resistant Acinetobacter baumannii contamination in an intensive care unit**. *Revista da Sociedade Brasileira de Medicina Tropical* 2017, **50**(2):167-172.
23. Garnacho-Montero J, Timsit JF: **Managing Acinetobacter baumannii infections**. *Current opinion in infectious diseases* 2019, **32**(1):69-76.
24. Metan G, Sariguzel F, Sumerkan B: **Factors influencing survival in patients with multi-drug-resistant Acinetobacter bacteraemia**. *European journal of internal medicine* 2009, **20**(5):540-544.
25. Al Jarousha AM, El Jadba AH, Al Afifi AS, El Qouqa IA: **Nosocomial multidrug-resistant Acinetobacter baumannii in the neonatal intensive care unit in Gaza City, Palestine**. *International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases* 2009, **13**(5):623-628.
26. Liang CA, Lin YC, Lu PL, Chen HC, Chang HL, Sheu CC: **Antibiotic strategies and clinical outcomes in critically ill patients with pneumonia caused by carbapenem-resistant Acinetobacter baumannii**. *Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases* 2018, **24**(8):908.e901-908.e907.