Intensive care unit-acquired *Acinetobacter baumannii* infections in a Moroccan teaching hospital: epidemiology, risk factors and outcome

Jean Uwingabiye^{1*}, Abdelhay Lemnouer², Sabina Baidoo³, Mohammed Frikkh⁴, Jalal Kasouati⁵, Adil Maleb⁶, Yassine Benlahlou⁷, Fatna Bssaibis⁸, Albert Mbayo⁹, Nawfal Doghmi¹⁰, Khalil Abouelalaa¹¹, Abdelouahed Baite¹², Azeddine Ibrahimi¹³, Mostafa Elouennass¹⁴

Abstract

Introduction The objective of this study was to examine the epidemiology, risk factors and outcome associated with *Acinetobacter baumannii* infections in the intensive care units (ICUs) in a Moroccan teaching hospital.

Methods This is a matched case-control study conducted as a joint collaboration between the clinical Bacteriology department and the two ICUs of Mohammed V Military Teaching Hospital from January 2015 to July 2016.

Results Among 964 patients hospitalized in the ICUs, 81 (8.4%) developed *A. baumannii* infections. Multivariate logistic regression analysis identified the following independent risk factors for ICU-acquired *A. baumannii* infections: ICU stay ≥ 14 days (odds ratio (OR)=6.4), prior use of central venous catheters (OR=18), prior use of mechanical ventilation (OR=9.5), duration of invasive procedures ≥ 7 days (OR=7.8), previous exposure to imipenem (OR=9.1), previous exposure to amikacin (OR=5.2), previous exposure to antibiotic polytherapy (OR=11.8) and previous exposure to corticotherapy (OR=5). On the other hand, the admission for post-operative care was identified as a protective factor. The crude mortality in patients with *A. baumannii* infection was 74.1%. Multivariate analysis showed that septic shock (OR=19.2) and older age (≥ 65 years) (OR=4.9) were significantly associated to mortality risk in patients with *A. baumannii* infection.

Conclusion Our results show that shortening the ICU stay, rational use of medical devices and optimizing antimicrobial therapy could reduce the incidence of these infections. Elderly patients and those with septic shock have a poor prognosis. These findings highlight the need for focusing on the high-risk patients to prevent these infections and improve clinical outcome.

Keywords *Acinetobacter baumannii*, epidemiology, risk factors, infection, intensive care unit, prognostic factor

Introduction

Acinetobacter baumannii is globally recognized as a main nosocomial pathogen, causing severe infections in critically ill patients hospitalized in

intensive care units (ICUs). International studies have shown that *Acinetobacter* spp. infections represent 7.9% of ventilator-associated

Received: 30 August 2017; revised: 25 October 2017; accepted: 01 December 2017.

¹PharmD, Department of Clinical Bacteriology, Mohammed V Military Teaching Hospital, Research Team of Epidemiology and Bacterial Resistance, Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, avenue Mohamed Belarbi El Alaoui, B.P. 6203, Rabat, Morocco; ²MD, Department of Clinical Bacteriology, Mohammed V Military Teaching Hospital, Research Team of Epidemiology and Bacterial Resistance, Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, avenue Mohamed Belarbi El Alaoui, B.P. 6203, Rabat, Morocco; ³PharmD, Department of Clinical Bacteriology, Mohammed V Military Teaching Hospital, Research Team of Epidemiology and

Bacterial Resistance, Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, avenue Mohamed Belarbi El Alaoui, B.P. 6203, Rabat, Morocco; ⁴MD, Department of Clinical Bacteriology, Mohammed V Military Teaching Hospital, Research Team of Epidemiology and Bacterial Resistance, Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, avenue Mohamed Belarbi El Alaoui, B.P. 6203, Rabat, Morocco; ⁵MD, Department of Clinical Bacteriology, Mohammed V Military Teaching Hospital, Research Team of Epidemiology and Bacterial Resistance, Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, avenue Mohamed Belarbi El Alaoui, B.P. 6203, Rabat, Morocco;

pneumonia and 5.7 to 15.7% of bloodstream infections in the ICUs.^{1,2}

In Moroccan ICUs, *Acinetobacter* spp. represented 24.85% of all isolates and 31.5% of all Gram-negative rods.³ A recently published study demonstrated that the clonal spread of the clinical *A. baumannii* isolates was related to those isolated from the hospital environment in two Moroccan ICUs.⁴ The same research team reported also that the clinical *A. baumannii* isolates were more resistant to the antiseptics and disinfectants than the environmental ones.⁵

This microorganism has also become a matter of great concern due to its extraordinary capability of acquiring resistance to commonly used antibiotics. However, polymyxins remain the last therapeutic option but the emergence of colistin-resistant *A. baumannii* isolates has been reported all over the world.⁶ During the past decade, the antibiotic resistance rates of *A. baumannii* strains increased from 78.3 to 95.7% for piperacillin/tazobactam, 68.7 to 95.8% for ceftazidime, 31.4 to 87.7% for imipenem, 27.3 to 59.3% for amikacin and 77.8 to 96.6% for

ciprofloxacin in Moroccan ICUs.^{3,7}

Reported risk factors for acquiring *A. baumannii* infections include: invasive procedures, causes of hospitalization, host factors, length of ICU stay and prior use of broad-spectrum antimicrobial agents.⁶

These infections are associated with a mortality ranging from 28.3 to 84.3% in the ICU.^{7,8} Based on the literature data, the independent predictor factors of mortality vary from country to country and from region to region, and they may be related to the ICU-acquired infections, ineffective empirical antimicrobial therapy, extent of antimicrobial resistance, immunosuppression, severe sepsis, septic shock, use of medical devices, admission from other healthcare facilities and steroid use.⁸⁻¹¹

To the best of our knowledge, no study on the risk factors or/and prognostic factors associated with *A. baumannii* infection has been carried out in our region. That is why it was deemed necessary to carry out this study whose aim was to examine the epidemiology, risk factors and

⁶PharmD, Department of Clinical Bacteriology, Mohammed V Military Teaching Hospital, Research Team of Epidemiology and Bacterial Resistance, Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, avenue Mohamed Belarbi El Alaoui, B.P. 6203, Rabat, Morocco;

⁷PharmD, Department of Clinical Bacteriology, Mohammed V Military Teaching Hospital, Research Team of Epidemiology and Bacterial Resistance, Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, avenue Mohamed Belarbi El Alaoui, B.P. 6203, Rabat, Morocco;

⁸Msc, Department of Clinical Bacteriology, Mohammed V Military Teaching Hospital, Research Team of Epidemiology and Bacterial Resistance, Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, avenue Mohamed Belarbi El Alaoui, B.P. 6203, Rabat, Morocco;

⁹MD, Department of Intensive Care Units, Mohammed V Military Teaching Hospital, Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, avenue Mohamed Belarbi El Alaoui, B.P. 6203, Rabat, Morocco;

¹⁰MD, Department of Intensive Care Units, Mohammed V Military Teaching Hospital, Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, avenue Mohamed Belarbi El Alaoui, B.P. 6203, Rabat, Morocco;

¹¹MD, Department of Intensive Care Units, Mohammed V Military Teaching Hospital, Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, avenue Mohamed Belarbi El Alaoui, B.P. 6203, Rabat, Morocco;

¹²MD, Department of Intensive Care Units, Mohammed V Military Teaching Hospital, Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, avenue Mohamed Belarbi El Alaoui, B.P. 6203, Rabat, Morocco;

¹³PhD, Medical Biotechnology Laboratory, Faculty of Medicine and Pharmacy, Mohammed V University, avenue Mohamed Belarbi El Alaoui, B.P. 6203, Rabat, Morocco;

¹⁴MD, Department of Clinical Bacteriology, Mohammed V Military Teaching Hospital, Research Team of Epidemiology and Bacterial Resistance, Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, avenue Mohamed Belarbi El Alaoui, B.P. 6203, Rabat, Morocco.

*Corresponding author: Jean Uwingabiye, PharmD, Department of Clinical Bacteriology, Mohammed V Military Teaching Hospital, Research Team of Epidemiology and Bacterial Resistance, Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, avenue Mohamed Belarbi El Alaoui, B.P. 6203, Rabat, Morocco. uwije2020@yahoo.fr

outcome associated with *A. baumannii* infections in ICUs in a Moroccan teaching hospital.

Methods

Study design and setting

This is a 1:2 matched case-control study conducted as a joint collaboration between the clinical Bacteriology department and the two ICUs of Mohammed V Military Teaching Hospital from January 2015 to July 2016. The two ICUs (medical and surgical) of our hospital have ten beds each and treat approximately 600-700 patients per year.

Case patients were defined as patients infected by *A. baumannii* according to the Centers for Disease Control and Prevention criteria.¹² The infection was considered as ICU-acquired if it occurred 48 hours following ICU admission. The patients who were colonized with *A. baumannii* were excluded.

Every case-patient was matched with two control-patients based on ward, age, sex and period of admission. Controls were defined as patients hospitalized in the ICUs without *A. baumannii* infections. The controls were chosen from the patients who stayed in the same ward in the same period as case-patients.

For each patient, clinical and microbiological data were collected from patient records and from computer medical databases. Patient variables considered included gender, age, length of ICU stay, underlying disease, use of invasive procedures, sampling site, bacterial co-infection, antimicrobial susceptibility profile, antibiotic pretreatment, targeted antibiotic therapy, appropriate antibiotic therapy, corticosteroid therapy and the clinical outcome.

Appropriate antimicrobial treatment was defined as the use of antimicrobial agent to which *A. baumannii* is susceptible in respect of the dosage, route of administration and duration of treatment. When antibiotic therapy did not meet any of these criteria, it was considered to be inappropriate.

Microbiological testing

The microbiological methods were part of routine laboratory activity. The isolation of all *A.*

baumannii isolates from clinical specimens was performed on blood agar and on bromocresol purple lactose agar. The identification was done using routine bacteriological tests based on morphological, culture and biochemical characteristics (Gram staining, ApI 20NE). The routine antibiotic susceptibility testing was carried out by using the agar disk diffusion method according to the guidelines of the Antibiogram Committee of the French Society of Microbiology and the European Committee for Antimicrobial Susceptibility Testing. The minimum inhibitory concentrations of colistin were determined by E-test method and confirmed by Sensititre™ Gram Negative MIC Plate (GNX3F) according to the manufacturer's instructions.

The *A. baumannii* isolates were divided into different categories according to their antibiotic resistance.¹³ The multidrug-resistant (MDR) isolates were defined as resistant to three or more of the following antibiotics: aminoglycosides, antipseudomonal beta-lactam, antipseudomonal beta-lactam-beta-lactamase inhibitor combination, fluoroquinolones, trimethoprim-sulfamethoxazole, and polymyxins. The extensively drug-resistant (XDR) isolates were defined as resistant to all antibiotics except colistin.

Statistical analysis

The data were entered into Microsoft Office Excel 2013. Statistical analysis was performed using the SPSS version 13 software (SPSS Inc., Chicago, IL, USA). Quantitative variables were expressed as mean $\pm$ standard deviation or as median (interquartile range - IQR) and qualitative variables as percentage. The comparison of the qualitative variables was carried out by the Pearson Chi-square and Fisher exact tests and the quantitative variables by the t student and Mann-Whitney U tests according to the distribution normality. Multivariate analysis was performed using a logistic regression model. The odds ratio (OR) and their corresponding 95% confidence intervals (CIs) for each variable were also calculated. All statistical tests were two-tailed; a p value <0.05 was considered statistically significant.

Results

Patient characteristics

Among 964 patients hospitalized in the ICU during the study period, 81 (8.4%) developed *A. baumannii* infections. Out of the infected patients, 55 (67.9%) were male with a male/female sex ratio of 2.1 and their mean age was 56.75 ± 20.7 years. The median duration of ICU stay before infections was 9 (IQR: 5-13.3) days. Broncho-pulmonary infections were the most common (54/81=66.7%) followed by septicemia (23/81=28.4%), urinary tract infections (2/81=2.5%) and surgical site infections (2/81=2.5%). Co-infection was found in 46 (56.79%) patients with *A. baumannii* infections. The most prevalent co-isolates were *Pseudomonas* spp. (n=21, 35%), *Staphylococcus aureus* (n=8, 13.3%) and *Klebsiella pneumoniae* (n=7, 11.9%) (Table 1).

Table 1. The distribution of bacterial co-infections in patients with *A. baumannii* infections

Parameters	N	%
Gram-negative bacilli	42	71.1
Non-fermenting Gram-negative bacilli	22	37.2
<i>Pseudomonas</i> spp.	21	35.6
<i>Stenotrophomonas maltophilia</i>	1	1.7
Enterobacteriaceae	18	30.5
<i>Escherichia coli</i>	4	6.7
<i>Klebsiella pneumoniae</i>	7	11.9
<i>Enterobacter</i> spp.	4	6.7
<i>Serratia</i> spp.	1	1.7
<i>Proteus</i> spp.	2	3.4
Other Gram-negative bacilli	2	3.4
<i>Haemophilus influenzae</i>	2	3.4
Gram-positive cocci	13	22
<i>Staphylococcus aureus</i>	8	13.5
Coagulase-negative staphylococci	2	3.4
<i>Enterococcus faecalis</i>	1	1.7
<i>Streptococcus</i> spp.	2	3.4
Gram-positive bacilli	4	6.7
<i>Corynebacterium</i> spp.	4	6.7
Total	59	100

The rate of MDR and XDR were 77 (95.1%) and 38 (46.9%), respectively. The antimicrobial resistance pattern is represented in Figure 1 (appendix).

Risk factors for ICU acquired *A. baumannii* infections

The variables that were found to be statistically significant in univariate analysis were: admission for polytrauma, emergency hospitalization before admission to ICU, longer length of ICU stay, prior use of arterial catheters, history of septic shock, prior use of empirical antibiotic therapy, prior use of third generation cephalosporins, prior use of imipenem, previous use of amikacin, previous use of colistin, previous use of glycopeptide antibiotics, administration of more than two antibiotics prior to infections, previous corticotherapy, and duration of empirical antibiotic treatment ≥ 5 days. On the other hand, the admission for post-operative care was identified as a protective factor (Table 2 - appendix). Meanwhile, multivariate logistic regression analysis identified the following independent risk factors for intensive care unit-acquired *A. baumannii* infections: longer length of ICU stay (≥ 14 days) (OR=6.4), prior use of central venous catheters (OR=18), prior use of mechanical ventilation (OR=9.5), duration of invasive procedures ≥ 7 days (OR=7.8), previous exposure to imipenem (OR=9.1), previous exposure to amikacin (OR=5.2), previous exposure to antibiotic polytherapy (OR=11.8) and previous exposure to corticotherapy (OR=5) – Table 3 (Appendix).

Antibiotic treatment of ICU acquired *A. baumannii* infections

Among infected patients, 60 (80.5%) received the appropriate antibiotic treatment after the occurrence of *Acinetobacter* infections. The median antibiotic treatment duration was 10 [IQR, 5-15] days. Colistin was the most commonly used antibiotic (n=55, 67.9%) in targeted antibiotic therapy followed by amikacin (n=18, 22.2%). The combination antibiotic therapy regimens were prescribed in 18 cases (22.2%). The most frequently combined

antibiotics were colistin plus amikacin (n=11, 13.58%) and colistin plus rifampicin (n=4, 4.94%). The remaining associated antibiotics were as follows: colistin plus gentamicin (1.23%), amikacin plus imipenem (1.23%) and moxifloxacin plus ceftriaxone (1.23%).

Outcome

The crude mortality rate in patients with *A. baumannii* (74.1%) was significantly higher than that of control patients (27.3%) ($p < 0.0001$). The median duration of hospitalization after diagnosis of *Acinetobacter* infection was 10 (IQR=2-17) days. Table 4 (appendix) summarizes univariate analysis of risk factors for mortality in patients infected with *A. baumannii*. The multivariate analysis revealed that the independent risk factors for mortality among infected patients with *A. baumannii* were septic shock (OR=19.2) and age ≥ 65 years (OR=4.9) (Table 5 - appendix).

Discussion

A. baumannii continues to be one of the most troublesome pathogens causing nosocomial infections in ICU patients. In our study, the incidence of ICU-acquired *A. baumannii* infections (8.4%) was lower than that reported in India (10%)¹⁴ and higher than that observed in Mexican patients with cancer (4.6%).¹⁵ This variability in incidence rates could be explained by differences in the reinforcement and compliance of infection control measures, especially hand hygiene practices and the decontamination of hospital environment.

In the current study, the independent risk factors for acquiring these infections can be classified into three categories: those related to the increased length of ICU stay, those related to the use of invasive medical devices (use of central venous catheters or mechanic ventilation and invasive procedures ≥ 7 days) and those related to previous drug therapy (imipenem, amikacin, antibiotic polytherapy and corticosteroids). Our study differs from the related previous studies by case mix groups, anatomic site of infection, antibiotic treatment protocols and antibiotic resistance profile. According to literature data,

the risk factors vary across countries and between regions; the most commonly reported risk factors are prior exposure to carbapenems, previous antimicrobial therapy, central venous catheter insertion and maintenance of mechanical ventilation while the others such as respiratory failure at admission in the ICU, immunosuppression including prior receipt of chemotherapy, previous sepsis in the ICU, low albumin level, prior surgeries, previous use of Foley catheter, prior hospitalization, receipt of total parenteral nutrition, prolonged hospitalization and neutropenia are rarely described.^{6,16-21}

Our findings show that patients who spent 14 days or more in the ICU had over six-fold increased risk of ICU-acquired *A. baumannii* infections, suggesting that ICU-acquired *A. baumannii* infections are due to prolonged ICU stay. Moreover, the median length of ICU stay of patients who developed ICU acquired *A. baumannii* infection was longer than that of other patients (18 (IQR: 10-26) days vs. 3 (IQR: 1-6) days, $p < 0.0001$) in this study, testifying that these infections were also responsible for a significantly longer ICU stay. Unnecessary hospitalization days may increase hospital acquired complications and economic burden.^{22,23}

In our study, multivariate analysis demonstrated that the use of mechanic ventilation and central venous catheters increased 9 and 18 times respectively, the risk for acquisition of *A. baumannii* infections compared to control patients. Medical devices are indispensable to modern medicine in the management of patients but their presence is associated with infection risks. Previous authors identified mechanic ventilation as a potential risk factor for ventilator-associated pneumonia and bacteremia.^{6,8,24} This explains why *A. baumannii* isolates were most commonly found in the respiratory tract (66.7%) and in the bloodstream (28.4%). Similar to our findings, the insertion of central venous catheters has also been reported to be independently associated with MDR *A. baumannii* bacteremia in a Korean study.²⁴ Indeed, catheters are important sources of bloodstream infections. The insertion of the

catheter into the organism, leads to the constitution of biofilm thus causing local and/ or systemic infection within 24 hours of its insertion. On the other hand, the use of invasive procedures for 7 days or more increased the risk of ICU-acquired *A. baumannii* by almost 7-fold in this study. These findings suggest the need for the withdrawal of medical devices as soon as possible to prevent development of ICU acquired *A. baumannii* infections especially when they are no longer deemed necessary.

Our results also show that imipenem and amikacin increased the risk for *A. baumannii* infections by 9.1 and 5.2 respectively. These results are disturbing because both antibiotics are commonly used for empirical antibiotic therapy and for treatment of *A. baumannii* infections after diagnosis. The injudicious use of broad-spectrum antibiotics contributed to the selection of multi-drug resistant organisms.²⁵ Previous exposure to carbapenem, third generation cephalosporins and piperacillin-tazobactam have been reported as potential risk factors for MDR *Acinetobacter* infections.^{26,27}

In several studies including the current one, colistin remains the most active antibiotic against MDR *A. baumannii* and it is also the last option for the treatment of these infections.^{6,13,28} This explains why it was the most used antibiotic (67.9%) for the treatment of these infections in our study.

In the current study, combination antibiotic therapy was prescribed in 22.2% of infected patients. Previous studies showed that antibacterial combinations may prevent emerging resistance and preserve the activity of antibiotics in treating MDR *A. baumannii* infections. In addition, other researchers demonstrated that the mortality rate was lower in patients treated with combination antibiotic therapy than in those that received monotherapy.^{2,29} There are no particular guidelines for combination antibiotic therapy against these infections due to the absence of controlled clinical trials.²⁹ Current studies regarding the synergy or combination therapy for MDR *A. baumannii* infections were performed on animal models, uncontrolled small case series and in vitro studies.²¹ The combination therapy

prescribed in our ICUs was chosen based on the antibiotic resistance profiles, availability and costs of antibiotics, bacterial profiling and patient's clinical status.

The most commonly prescribed antibiotic combination was colistin plus amikacin (22.2%). Both antibiotics are known to be associated with an increased risk of nephrotoxicity.^{25,29} These results emphasize the importance of therapeutic drug monitoring of colistin and amikacin for optimizing the antibiotic therapy. Other colistin-based combined therapies used in our ICUs were colistin plus rifampicin and colistin plus gentamicin. In vivo and in vitro synergistic effects were found in the reports examining the combination of colistin and rifampicin, minocycline, carbapenem, sulbactam, tigecycline, daptomycin, fusidic acid and teicoplanin for treatment of *A. baumannii* infections. The following combination therapy: imipenem plus amikacin and moxifloxacin plus ceftriaxone were used for treatment of infections due to imipenem susceptible *A. baumannii* isolates.³⁰

Likewise, our study demonstrates that receiving antibiotic polytherapy independently increased the risk of *A. baumannii* infections by 11.8 times. Combination therapy leads to higher selective pressure of antibiotics on the gut flora than monotherapy and causes the proliferation of resistant strains.² Furthermore, the use of antibacterial combinations can expose to more adverse effects and complications than a single antibiotic.²⁵

In this study, the use of corticoids independently increased the risk of ICU acquired *A. baumannii* by 5 times. Corticosteroids weaken the immune systems and lead to a higher risk of infections. In a Spanish study, immunosuppression was independently associated with *A. baumannii* nosocomial bacteremia.²⁰

Surprisingly, the admission for post-operative care was found to be a protective factor. This demonstrates the effort made by healthcare professionals to prevent postoperative nosocomial infections due to MDR *A. baumannii*.

In the present study, the mortality rate in patients with *A. baumannii* was more than two

times higher than in the control patients (74.1% vs 27.4%, $p < 0.0001$). The mortality rate found in case patients (74.1%) is comparable to that of the literature, which varies from 28.3 to 84.3%.^{8,9} Septic shock was significantly associated with a 19.2-fold increased risk of death. Septic shock remains the main cause of death in patients with *A. baumannii* infections in the ICU.³¹ Our results also demonstrate that old age (≥ 65 years) was independently associated with a 4.9-fold increased risk of mortality in patients with acquired ICU *A. baumannii* infection. The elderly critically ill patients are predisposed to high mortality due to organ system dysfunction, increased risk of septic shock in these patients, chronic co-morbidities, extended length of hospitalization and adverse drug reaction.³² The independent predictors of mortality reported in previously published studies and which were not identified in our study were: length of ICU stay, duration of intubation, inappropriate use of antibiotics after diagnosis of the infection, presence of malignancy, need for mechanical ventilation, resistance to carbapenems, recent surgery, acute respiratory failure and acute renal failure.^{8-11,14,16,19,23}

Conclusion

Our results show that shortening the ICU stay, rational use of medical devices and optimization of initial empiric antibiotic therapy could significantly reduce the incidence of these infections. Elderly patients and those with septic shock have a poor prognosis. These findings highlight the need for focusing on the high-risk patients to prevent these infections and improve clinical outcome.

Authors' contributions statement: JU, SB, and ME conceived and designed the study, interpreted the results and wrote the manuscript. JU, SB, MF, JK, AMa, YB, FB, AMb, ND, KA and AB participated in data acquisition, literature search and in laboratory work. AI and AL were involved in critical revision of the manuscript. All authors read and approved final version of manuscript.

Conflicts of interest: All authors – none to disclose.

Funding: none to declare.

References

1. Kalanuria AA, Ziai W, Mirski M. Ventilator-associated pneumonia in the ICU. *Crit Care* 2014;18:208. [[Crossref](#)] [[PubMed](#)] [[FullText](#)]
2. Timsit JF, Soubirou JF, Voiriot G, et al. Treatment of bloodstream infections in ICUs. *BMC Infect Dis* 2014;14:489. [[Crossref](#)] [[PubMed](#)] [[FullText](#)]
3. Uwingabiye J, Frikh M, Lemnouer A, et al. *Acinetobacter* infections prevalence and frequency of the antibiotics resistance: comparative study of intensive care units versus other hospital units. *Pan Afr Med J* 2016;23:191. [[Crossref](#)] [[PubMed](#)] [[FullText](#)]
4. Uwingabiye J, Lemnouer A, Roca I, et al. Clonal diversity and detection of carbapenem resistance encoding genes among multidrug-resistant *Acinetobacter baumannii* isolates recovered from patients and environment in two intensive care units in a Moroccan hospital. *Antimicrob Resist Infect Control* 2017;6:99. [[Crossref](#)] [[PubMed](#)] [[FullText](#)]
5. Lanjri S, Uwingabiye J, Frikh M, et al. In vitro evaluation of the susceptibility of *Acinetobacter baumannii* isolates to antiseptics and disinfectants: comparison between clinical and environmental isolates. *Antimicrob Resist Infect Control* 2017;6:36. [[Crossref](#)] [[PubMed](#)] [[FullText](#)]
6. Lin MF, Lan CY. Antimicrobial resistance in *Acinetobacter baumannii*: From bench to bedside. *World J Clin Cases* 2014;2:787-814. [[Crossref](#)] [[PubMed](#)] [[FullText](#)]
7. Elouennass M, Bajou T, Lemnouer AH, Foissaud V, Hervé V, Baaj AJ. *Acinetobacter baumannii*: étude de la sensibilité des souches isolées à l'hôpital militaire d'instruction Mohammed V, Rabat, Maroc. *Med Mal Infect* 2003;33:361-4. [[Crossref](#)]
8. Punpanich W, Nithitamsakun N, Treeratweeraphong V, Suntarattiwong P. Risk factors for carbapenem non-susceptibility and mortality in *Acinetobacter baumannii* bacteremia in children. *Int J Infect Dis* 2012;16:e811-5. [[Crossref](#)] [[PubMed](#)]
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. *Am J Infect Control* 2014;42:206-8. [[Crossref](#)] [[PubMed](#)]
10. Townsend J, Park AN, Gander R, et al. *Acinetobacter* infections and outcomes at an academic medical center: a disease of long-term care. *Open Forum Infect Dis* 2015;2:ofv023. [[Crossref](#)] [[PubMed](#)] [[FullText](#)]
11. Liu Q, Li W, Du X, et al. Risk and prognostic factors for multidrug-resistant *Acinetobacter baumannii* complex bacteremia: a retrospective study in a tertiary hospital of west China. *PLoS One* 2015;10:e0130701. [[Crossref](#)] [[PubMed](#)] [[FullText](#)]
12. 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. *Am J Infect Control* 2008;36:309-32. [[Crossref](#)] [[PubMed](#)]

13. Magiorakos AP, Srinivasan A, Carey RB et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. *Clin Microbiol Infect* 2012;18:268-81. [[Crossref](#)] [[PubMed](#)]
14. Mathai AS, Oberoi A, Madhavan S, Kaur P. *Acinetobacter* infections in a tertiary level intensive care unit in northern India: epidemiology, clinical profiles and outcomes. *J Infect Public Health* 2012;5:145-52. [[Crossref](#)] [[PubMed](#)]
15. Namendys-Silva SA, Correa-García P, García-Guillén FJ, et al. Outcomes of critically ill cancer patients with *Acinetobacter baumannii* infection. *World J Crit Care Med* 2015;4:258-64. [[PubMed](#)] [[FullText](#)]
16. Cisneros JM, Rodríguez-Baño J, Fernández-Cuenca F, et al. Risk-factors for the acquisition of imipenem-resistant *Acinetobacter baumannii* in Spain: a nationwide study. *Clin Microbiol Infect* 2005;11:874-9. [[Crossref](#)] [[PubMed](#)]
17. Chopra T, Marchaim D, Johnson PC, et al. Risk factors and outcomes for patients with bloodstream infection due to *Acinetobacter baumannii-calcoaceticus* complex. *Antimicrob Agents Chemother* 2014;58:4630-5. [[Crossref](#)] [[PubMed](#)] [[FullText](#)]
18. Ardoino I, Zangirolami F, Lemmi D, et al. Risk factors and epidemiology of *Acinetobacter baumannii* infections in a university hospital in Northern Italy: A case-control study. *Am J Infect Control* 2016;44:1600-5. [[Crossref](#)] [[PubMed](#)]
19. Turkoglu M, Mirza E, Tunçcan OG, et al. *Acinetobacter baumannii* infection in patients with hematologic malignancies in intensive care unit: risk factors and impact on mortality. *J Crit Care* 2011;26:460-7. [[Crossref](#)] [[PubMed](#)]
20. García-Garmendia JL, Ortiz-Leyba C, Garnacho-Montero J, et al. Risk factors for *Acinetobacter baumannii* nosocomial bacteremia in critically ill patients: a cohort study. *Clin Infect Dis* 2001;33:939-46. [[Crossref](#)] [[PubMed](#)]
21. Manchanda V, Sanchaita S, Singh N. Multidrug resistant *Acinetobacter*. *J Glob Infect Dis* 2010;291-304. [[Crossref](#)] [[PubMed](#)] [[FullText](#)]
22. Arefian H, Hagel S, Heublein S, et al. Extra length of stay and costs because of health care-associated infections at a German university hospital. *Am J Infect Control* 2016;44:160-6. [[Crossref](#)] [[PubMed](#)]
23. Sunenshine RH, Wright MO, Maragakis LL, et al. Multidrug-resistant *Acinetobacter* infection mortality rate and length of hospitalization. *Emerg Infect Dis* 2007;13:97-103. [[Crossref](#)] [[PubMed](#)] [[FullText](#)]
24. Jung JY, Park MS, Kim SE, et al. Risk factors for multidrug resistant *Acinetobacter baumannii* bacteremia in patients with colonization in the intensive care unit. *BMC Infect Dis* 2010;10:228. [[Crossref](#)] [[PubMed](#)] [[FullText](#)]
25. Tamma PD, Cosgrove SE, Maragakis LL. Combination therapy for treatment of infections with gram-negative bacteria. *Clin Microbiol Rev* 2012;25:450-70. [[Crossref](#)] [[PubMed](#)] [[FullText](#)]
26. Ng TM, Teng CB, Lye DC, Apisarnthanarak A. A multicenter case-case control study for risk factors and outcomes of extensively drug-resistant *Acinetobacter baumannii* bacteremia. *Infect Control Hosp Epidemiol* 2014;35:49-55. [[Crossref](#)] [[PubMed](#)]
27. Lee SO, Kim NJ, Choi SH, et al. Risk factors for acquisition of imipenem-resistant *Acinetobacter baumannii*: a case-control study. *Antimicrob Agents Chemother* 2004;48:224-8. [[Crossref](#)] [[PubMed](#)] [[FullText](#)]
28. Lachhab Z, Frikh M, Maleb A, et al. Bacteraemia in intensive care unit: clinical, bacteriological, and prognostic prospective study. *Can J Infect Dis Med Microbiol* 2017;2017:4082938. [[Crossref](#)] [[PubMed](#)] [[FullText](#)]
29. Kassamali Z, Jain R, Danziger LH. An update on the arsenal for multidrug-resistant *Acinetobacter* infections: polymyxin antibiotics. *Int J Infect Dis* 2015;30:125-32. [[Crossref](#)] [[PubMed](#)]
30. Lee CR, Lee JH, Park M, et al. Biology of *Acinetobacter baumannii*: pathogenesis, antibiotic resistance mechanisms, and prospective treatment options. *Front Cell Infect Microbiol* 2017;7:55. [[Crossref](#)] [[PubMed](#)] [[FullText](#)]
31. del Mar Tomas M, Cartelle M, Pertega S, et al. Hospital outbreak caused by a carbapenem-resistant strain of *Acinetobacter baumannii*: patient prognosis and risk-factors for colonisation and infection. *Clin Microbiol Infect* 2005;11:540-6. [[Crossref](#)] [[PubMed](#)]
32. Nasa P, Juneja D, Singh O. Severe sepsis and septic shock in the elderly: An overview. *World J Crit Care Med* 2012;1:23-30. [[Crossref](#)] [[PubMed](#)] [[FullText](#)]

Please cite this article as:

Uwingabiye J, Lemnouer A, Baidoo S, Frikh M, Kasouati J, Maleb A, Benlahlou Y, Bsaibis F, Mbayo A, Doghmi N, Abouelalaa K, Baite A, Ibrahimi A, Elouennass M. Intensive care unit-acquired *Acinetobacter baumannii* infections in a Moroccan teaching hospital: epidemiology, risk factors and outcome. *GERMS* 2017;7(4):193-205. doi: 10.18683/germs.2017.1126

Appendix

Figure 1: In vitro antimicrobial susceptibility profiles of *A. baumannii* isolates

R – resistant; I – intermediate; S – susceptible; TIC – ticarcillin; PIP – piperacillin; TCC – ticarcillin / clavulanic acid; TZP – piperacillin/tazobactam; CAZ – ceftazidime; FEP – cefepime; IMP – imipenem; TOB – tobramycin; AK – amikacin; NET – netilmicin; CIP – ciprofloxacin; TET – tetracycline; SXT – sulfamethoxazole/trimethoprim; RD – rifampicin; CT – colistin.

Table 2. Comparison of demographics and clinical characteristics of patients with ICU acquired *A. baumannii* infections (cases) and control patients in univariate analysis.

Parameters	Total N=243	Cases N=81	Controls N=162	P	OR	95%CI
Male sex, N (%)	159 (65.4)	55 (67.9)	104 (64.2)	0.567	0.8	0.5-1.5
Mean age (years), mean ± SD	58.52±19.5	56.75±20.7	59.4±18.9	0.321	1	1-1.1
Median length of ICU stay, median [IQR]	5 [2-14]	18 [10-26]	3 [1-6]	<0.0001	20.9	10.2-42.8
ICU stay ≥14days, N (%)	61 (25.1)	51 (63)	10 (6.2)	<0.0001	25.9	11.8-56.5
Causes of hospitalization	N (%)	N (%)	N (%)			
Respiratory distress	48 (19.8)	16 (19.8)	32 (19.8)	1	1	0.5-2
Consciousness disorder	24 (9.9)	9 (11.1)	15 (9.3)	0.572	1.4	0.5-4
Polytrauma	27 (11.1)	18 (22.2)	9 (5.6)	<0.0001	4.9	2.1-11.4
Post-operative care	65 (26.7)	10 (12.3)	55 (34)	<0.0001	0.3	0.1-0.6
Acute pancreatitis	9 (3.7)	4 (4.9)	5 (3.1)	0.471	1.6	0.4-6.2
Department stay prior to ICU admission	N (%)	N (%)	N (%)			
Emergency	148 (60.9)	59 (72.8)	89 (54.9)	0.007	2.2	1.2-3.9
Medical department	34 (14)	8 (9.9)	26 (16)	0.191	0.6	0.2-1.3
Surgical department	61 (25.1)	18 (22.2)	43 (26.5)	0.285	0.5	0.4-1.5
Underlining disease	N (%)	N (%)	N (%)			

Parameters	Total N=243	Cases N=81	Controls N=162	P	OR	95%CI
Diabetes	69 (28.4)	17 (21)	52 (32.1)	0.07	0.6	0.3-1.1
High blood pressure	72 (29.6)	21 (25.9)	51 (31.5)	0.371	0.8	0.4-1.4
Chronic renal failure	9 (3.7)	4 (4.9)	5 (3.1)	0.471	1.6	0.4-6.2
Chronic obstructive pulmonary disease	26 (10.7)	7 (8.6)	19 (11.7)	0.463	0.7	0.3-1.8
Chronic smoking	41 (16.9)	13 (16)	28 (17.3)	0.809	0.9	0.4-1.9
Alcohol abuse	4 (1.6)	2 (2.5)	2 (1.2)	0.602	2.1	0.3-14.6
Malignant hemopathies	8 (3.3)	4 (4.9)	4 (2.5)	0.309	2.1	0.5-8.4
Previous exposure to invasive procedures	N (%)	N (%)	N (%)			
Arterial catheters	47 (19.3)	26 (32.1)	21 (13)	<0.0001	3.2	1.6-6.1
Central venous catheters	59 (24.3)	42 (51.9)	17 (10.5)	<0.0001	9.2	4.7-17.9
Peripheral venous catheters	54 (22.2)	21 (25.9)	33 (20.4)	0.326	1.4	0.7-2.6
Urinary catheter	78 (32.1)	50 (61.7)	28 (17.3)	<0.0001	7.7	4.2-14.1
Nasogastric tube	14 (5.8)	9 (11.1)	5 (3.1)	0.018	3.9	1.3-12.1
Mechanical ventilation	105 (43.2)	60 (74.1)	45 (27.8)	<0.0001	7.4	4.1-13.6
Chest tube	11 (4.5)	4 (4.9)	7 (4.3)	0.827	1.1	0.3-4
Recent surgery	45 (18.5)	12 (14.8)	33 (20.4)	0.293	0.7	0.3-1.4
Parenteral nutrition	62 (25.5)	45 (55.6)	17 (10.5)	<0.0001	1.2	5.5-20.8
Dialysis	8 (3.3)	3 (3.7)	5 (3.1)	0.799	1.2	0.3-5.2
Hemodialysis	8 (3.3)	4 (4.9)	4 (2.5)	0.309	2.1	0.5-8.4
Invasive procedures ≥7 days	81 (52.6)	61 (81.4)	20 (25)	<0.0001	14.1	6.4-30.8
Clinical complications	N (%)	N (%)	N (%)			
Sepsis	6 (2.5)	3 (3.7)	3 (1.9)	0.381	2	0.4-10.3
Severe sepsis	11 (4.5)	6 (7.4)	5 (3.1)	0.187	2.5	0.7-8.5
Septic shock	93 (38.3)	55 (67.9)	38 (23.5)	<0.0001	6.9	3.8-12.5
Empirical antibiotic therapy	N (%)	N (%)	N (%)			
Penicillins	52 (21.4)	18 (22.2)	34 (21)	0.825	1.1	0.6-2.1
Third generation cephalosporins	89 (36.6)	38 (46.9)	51 (31.5)	0.019	1.9	1.1-3.3
Imipenem	94 (38.7)	62 (76.5)	32 (19.8)	<0.0001	13.3	7-25.2
Amikacin	84 (34.6)	49 (60.5)	35 (21.6)	<0.0001	5.6	3.1-9.9
Gentamicin	15 (6.2)	7 (8.6)	8 (4.9)	0.258	1.8	0.6-5.2
Quinolones	33 (13.6)	9 (11.1)	24 (14.8)	0.427	0.7	0.3-1.6
Glycopeptide antibiotics	18 (7.4)	14 (17.2)	4 (2.5)	<0.0001	7.6	2.4-24
Metronidazole	32 (13.2)	12 (14.8)	20 (12.3)	0.592	1.2	0.6-2.7
Combination antibiotic therapy	N (%)	N (%)	N (%)			
Mono-antimicrobial therapy	40 (16.5)	9 (11.1)	31 (19.1)	0.112	0.5	0.2-1.2
Bi-antimicrobial therapy	53 (21.8)	17 (21)	36 (22.2)	0.826	0.9	0.5-1.8
Antibiotic polytherapy	94 (38.7)	50 (61.7)	44 (27.2)	<0.0001	4.3	2.4-7.6
Corticotherapy	107 (44)	50 (61.7)	57 (35.2)	<0.0001	3	1.7-5.2
Empirical antibiotic treatment ≥5 days	105 (54.4)	66 (82.5)	39 (34.5)	<0.0001	8.9	4.5-17.9
Mortality rate	105 (43.2)	60 (74.1)	45 (27.3)	<0.0001	7.4	4.1-13.6

ICU – intensive care unit; IQR – interquartile range; OR – odds ratio; SD – standard deviation; 95%CI – 95% confidence interval.

Table 3. Multivariate logistic regression analysis of the factors influencing ICU acquired *Acinetobacter* infections

Parameters	p	OR	95%CI
Duration of ICU stay ≥14 days	0.048	6.4	1.1-41
Admission for polytrauma	0.266	3.9	0.3-44.5
Previous hospitalization in Emergency department	0.353	0.5	0.1-2.3
Prior exposure to arterial catheters	0.060	0.2	0.1-1.1
Previous use of central venous catheters	0.006	18	2.3-141.5
Previous exposure to urinary catheter	0.152	0.3	0.1-1.5
Prior use of nasogastric tube	0.150	6.9	0.5-95.5
Previous exposure to mechanical ventilation	0.003	9.5	2.1-42.6
Previous exposure to parenteral nutrition	0.411	1.9	0.4-9.1
Duration of invasive procedures ≥7 days	0.033	7.8	1.2-51.2
History of septic shock	0.919	0.9	0.2-3.8
Prior use of antibiotic therapy	0.286	2.4	0.5-12.4
Previous use of third generation cephalosporins	0.066	4.2	0.9-19.5
Prior exposure to imipenem	0.012	9.1	1.6-51.5
Prior use of amikacin	0.027	5.2	1.2-22.4
Prior use of glycopeptide antibiotics	0.279	3.6	0.4-37.4
Prior exposure to antibiotic polytherapy	0.003	11.8	2.3-60.3
Duration of empirical antibiotic treatment ≥5 days	0.324	0.4	0.1-2.8
Previous corticotherapy	0.029	5	1.2-21.3

ICU – intensive care unit; IQR – interquartile range; OR – odds ratio; 95%CI – 95% confidence interval.

Table 4. Univariate analysis of risk factors for mortality in patients infected with *A. baumannii*

Variables	Deceased N=60	Survivors N=21	p
Male sex, N (%)	39 (65)	16 (76.2)	0.344
Mean age (years), mean±SD	60.4±19.2	46.63±21.7	0.362
Age ≥65 years, N (%)	27 (45)	4 (19)	0.035
Median duration of hospitalization before diagnosis of infection, median [IQR]	7.5 [4.25-12]	7 [4.5-12]	0.838
ICU stay ≥14days, N (%)	35 (58.3)	16(76.2)	0.145
Causes of hospitalization	N (%)	N (%)	
Respiratory distress	13 (21.7)	3 (14.3)	0.543
Consciousness disorder	10 (16.7)	3 (14.3)	1
Polytrauma	13 (21.7)	5 (23.8)	0.839
Post-operative care	7 (11.7)	3 (14.3)	0.714
Department stay prior to ICU admission	N (%)	N (%)	
Emergency	42 (70)	17 (81)	0.331
Medical department	7 (11.7)	1 (4.8)	0.673
Surgical department	11 (11.8)	3 (14.3)	1
Underlining disease	N (%)	N (%)	

Variables	Deceased	Survivors	p
Diabetes	13 (21.7)	4 (19)	0.8
High blood pressure	17 (28.3)	4 (19)	0.403
Chronic renal failure	3 (5)	1 (4.8)	1
Chronic obstructive pulmonary disease	4 (6.7)	3 (14.3)	0.368
Chronic smoking	10 (16.7)	3 (14.3)	1
Alcohol abuse	2 (3.3)	0	1
Malignant hemopathies	4 (6.7)	0	0.568
Invasive procedures	N (%)	N (%)	
Arterial catheters	19 (31.7)	7 (33.3)	1
Central venous catheters	32 (53.3)	10 (47.6)	0.652
Peripheral venous catheters	16 (26.7)	5 (23.8)	0.797
Urinary catheter	38 (63.3)	12 (57.1)	0.615
Nasogastric tube	5 (8.3)	4 (19)	0.228
Mechanical ventilation	46 (76.7)	14 (66.7)	0.368
Recent surgery	7 (11.7)	5 (23.8)	0.282
Parenteral nutrition	34 (56.7)	11 (52.4)	0.734
Invasive procedures ≥ 7 days	45 (81.8)	16 (84.2)	1
Clinical complications	N (%)	N (%)	
Sepsis	3 (5)	0	0.564
Severe sepsis	4 (6.7)	2 (9.5)	0.647
Septic shock	50 (83.3)	5 (23.8)	<0.0001
Empirical antibiotic therapy	59 (98.3)	20 (95.2)	0.454
Beta lactam antibiotics	59 (98.3)	21 (100)	1
Aminoglycosides	41 (68.3)	12 (57.1)	0.353
Quinolones	7 (11.7)	2 (9.5)	0.788
Combination antibiotic therapy	N (%)	N (%)	
Mono-antimicrobial therapy	7 (11.7)	2 (9.5)	0.788
Bi-antimicrobial therapy	16 (26.7)	1 (4.8)	0.034
Antibiotic polytherapy	35 (58.3)	15 (71.4)	0.288
Corticotherapy	40 (66.7)	10 (47.6)	0.122
Empirical antibiotic treatment ≥ 5 days	49 (83.1)	17 (81)	1
Presence of co-infections with <i>A. baumannii</i>	33 (55)	13 (61.9)	0.582
Category of resistance	N (%)	N (%)	
MDR	57 (95)	20 (95.2)	0.965
XDR	27 (45)	11 (52.4)	0.56
Targeted antibiotic therapy, N (%)	49 (81.7)	16 (76.2)	0.4
Colistin, N (%)	40 (66.7)	15 (71.4)	0.687
Amikacin, N (%)	15 (25)	3 (14.3)	0.376
Duration of targeted antibiotic therapy,	10.58$\pm$7.9	15.53$\pm$11.4	0.059

ICU – intensive care unit; IQR – interquartile range; SD – standard deviation.

Table 5. Multivariate analysis of risk factors for mortality in patients with *A. baumannii* infection

Parameters	P	OR	95%CI
Septic shock	<0.0001	19.2	5.2-71.4
Age ≥65 years	0.031	4.9	1.1-21.1

OR – odds ratio; 95%CI – 95% confidence interval.