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

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## 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

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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, antimicrobial therapy, 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

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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 ± 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** |
| *Pseudomonas* spp. | 21 | 35.6 |
| *Stenotrophomonas maltophilia* | 1 | 1.7 |
| **Enterobacteriaceae** | **18** | **30.5** |
| *Escherichia coli* | 4 | 6.7 |
| *Klebsiella pneumoniae* | 7 | 11.9 |
| *Enterobacter* spp. | 4 | 6.7 |
| *Serratia* spp. | 1 | 1.7 |
| *Proteus* spp. | 2 | 3.4 |
| **Other Gram-negative bacilli** | **2** | **3.4** |
| *Haemophilus influenzae* | 2 | 3.4 |
| **Gram-positive cocci** | **13** | **22** |
| *Staphylococcus aureus* | 8 | 13.5 |
| Coagulase-negative staphylococci | 2 | 3.4 |
| *Enterococcus faecalis* | 1 | 1.7 |
| *Streptococcus* spp. | 2 | 3.4 |
| **Gram-positive bacilli** | **4** | **6.7** |
| *Corynebacterium* 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.

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## Appendix

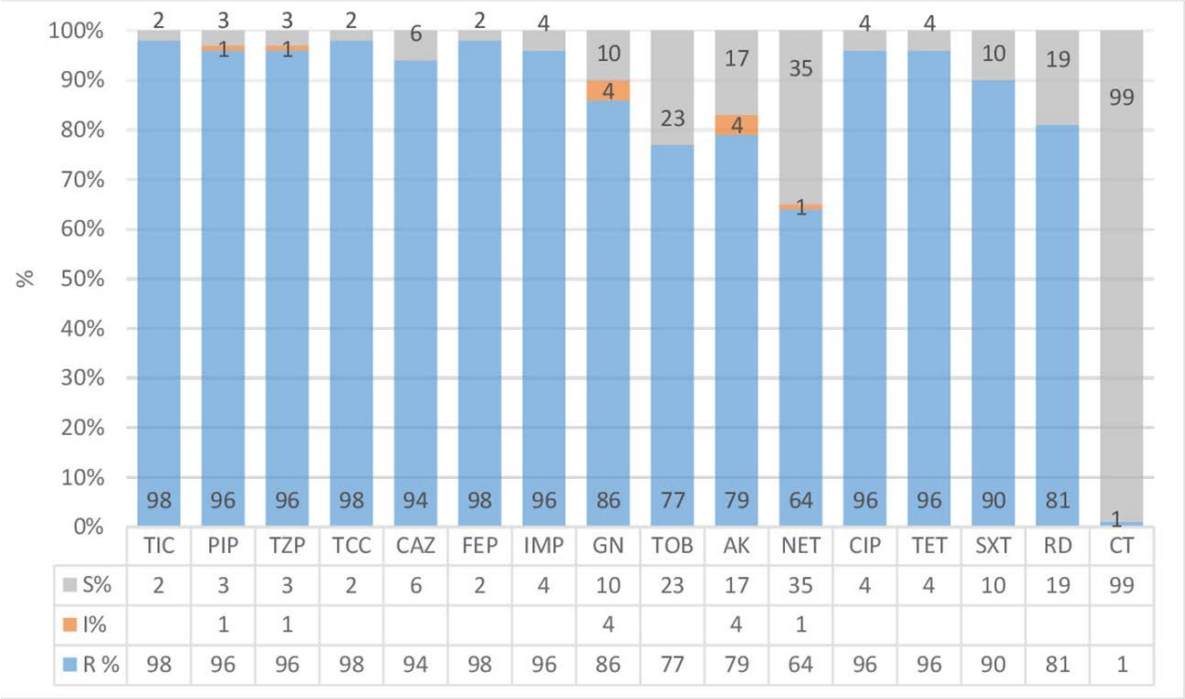



**Figure 1: In vitro antimicrobial susceptibility profiles of *A. baumannii* isolates**

**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** | 192 (79) | 79 (95.7) | 113 (69.8) | **<0.0001** | **17.1** | 4-72.5 |
| 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 | Survivors | p |
|---|---|---|---|
| | **N=60** | **N=21** | |
| **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 *A. baumannii*** | 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±7.9** | **15.53±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.