Acinetobacter baumannii Infection-Related Mortality in Hospitalized Patients: Risk Factors and Potential Targets for Clinical and Antimicrobial Stewardship Interventions

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Abstract: Due to resistance and scarcity of treatment options, nosocomial Acinetobacter baumannii infections are associated with significant fatality rates. We investigated the factors contributing to infection-related deaths to develop tailored stewardship interventions that could reduce these high mortality rates. We reviewed the medical records of adult inpatients with A. baumannii infections over two years. Patient demographics and clinical data were collected and statistically analyzed. The study included 321 patients with positive A. baumannii microbiological cultures, with respiratory infections accounting for 58.6%, soft tissues 29.3%, bacteremia 8.6%, urine 2.1%, and others 1.4%. The study population’s median (IQR) age was 62.6 (38.9–94.9) years, and hospital stay was 20 (9.5–40) days. Statistical analysis revealed that various risk factors contribute significantly to high in-hospital all-cause mortality (44%), as well as 14-day and 28-day mortality rates. Deaths increased by a factor of 1.04 with every additional year of age (p = 0.000), admission to the critical care unit (p = 0.000, OR: 2.86), and patients admitted with an infectious diagnosis had nearly three times the mortality rate as those admitted with other diagnoses (p = 0.000, OR: 3.12). Male gender (p < 0.001, OR: 2.14), any comorbid conditions (p = 0.000, OR: 5.29), prolonged hospitalization (>7 days) (p = 0.023, OR: 1.98), and hospital acquisition of infection (p = 0.027, OR: 1.68) were among the most significant predictors of mortality. All variables were investigated for their impact on all-cause, 14-day, and 28-day mortality rates. Improving multidisciplinary infection control practices, regular disinfection of patient care equipment, and optimal intubation practice that avoids unnecessary intubation are necessary interventions to reduce infection-related mortality rates. Better antibiotic selection and de-escalation, shorter hospital stays whenever possible, prompt medical stabilization of comorbid conditions, and fewer unnecessary admissions to critical care units will all lead to improved outcomes.

Keywords: Acinetobacter baumannii; risk factors; mortality; comorbidity; hospitalization; inpatients; MDR; critical care; history of hospitalization; history of infection; bloodstream infection; concurrent infections; antimicrobial stewardship

1. Introduction

Over the last two decades, Acinetobacter baumannii has been shown to develop a mounting resistance to nearly all available antibiotics. A. baumannii harbors the largest known pathogenicity island, consisting of 45 resistance genes, which enables horizontal gene transfer (HGT) via transposon migration and uptake, disseminating acquired antibiotic resistance to a wide range of antibiotics [1]. A. baumannii’s ability to modify its outer membrane, upregulate efflux pumps, form biofilms, colonize medical devices, and acquire...
Due to the significant increase in infection-related mortality rates due to limited antimicrobial options [3–5], the World Health Organization (WHO) designated carbapenem-resistant *A. baumannii* (CRAB) as a high-priority target for antibiotic research and development in 2017. [6]. Similarly, it was classified as a problematic pathogen by the Infectious Diseases Society of America (IDSA) [7]. Furthermore, according to the 2013 Centers for Disease Control and Prevention (CDC) report, multi-drug resistant (MDR) *A. baumannii* is a serious threat that causes approximately 7000 infections and 500 deaths each year in the United States. [8]

*A. baumannii* is a significant contributor to the increased rates of complicated hospital-acquired infections (HAI). According to the National Healthcare Safety Network (2008), *A. baumannii* is responsible for nearly 2% of all catheter-related bloodstream infections (BSIs) and 8% of ventilator-associated pneumonia (VAPs), with mortality rates ranging from 13 to 30% [9]. Many studies have linked chronic comorbid conditions, bedridden status, venous catheterization, intensive care unit (ICU) stay, infections with MDR phenotypes, concurrent fungal infection, and age to *A. baumannii* infection-related mortality [10–12].

Previous research by our group [13] found that patients infected with *A. baumannii* had high mortality and treatment failure rates. This study aims to identify risk factors contributing to poor clinical outcomes and higher mortality rates to provide evidence-based risk-mitigation recommendations for our national antimicrobial stewardship program.

### 2. Methods

#### 2.1. Study Population

We reviewed patients’ electronic medical records using the following inclusion criteria: adult inpatients (≥18 years) admitted to Suhar hospital (a referral hospital serving a third of national population) with clinical signs and symptoms of infection (to rule out colonization) and laboratory-confirmed identification of *A. baumannii* in infection-site samples. Only the first infection episode in two years (1 January 2018–31 December 2019) was chosen for patients with more than one positive culture. We examined the patients’ demographics, presenting symptoms, underlying comorbid conditions, prior hospitalization, and infection history.

We studied the hospitalization details, including admission diagnosis, discharge status, length of stay, admission ward, infection acquisition location, readmission rates, and microbiological information, including specimen type, susceptibility pattern, resistance phenotype, and concurrent infections. Patients with positive *A. baumannii* cultures who were not admitted or died prior to receiving one dose of antibiotics and pediatric patients were excluded from the study. The primary endpoints were all-cause in-hospital mortality, 14-day, and 28-day mortality before infection signs were resolved.

#### 2.2. Phenotype Categorization

Following the CLSI 2010 M100-S20 guidelines, all *A. baumannii* isolates resistant to at least one antibiotic from three or more antimicrobial classes were classified as MDR [14]. Carbapenemases producing isolates were detected phenotypically according to CLSI. Isolates with inhibition zones of <23 mm around (ertapenem 10 g or meropenem 10 g) and resistance to one or more third-generation cephalosporin (e.g., cefotaxime, ceftazidime, and ceftiraxone) were considered as carbapenem-resistant *A. baumannii* (CRAB). All penicillins, cephalosporins, carbapenems, and aztreonam were reported to be resistant in confirmed carbapenemase producing strains.

#### 2.3. Definitions

Chronic kidney disease is defined as an estimated glomerular filtration rate (eGFR) of <60 mL/min/1.73 m². Chronic respiratory diseases include chronic obstructive pulmonary disease, bronchiectasis, cystic fibrosis, and asthma. Cerebrovascular diseases include
intracranial stenosis, aneurysms, vascular malformations, thrombotic strokes, blockage (embolism), or hemorrhagic strokes. Chronic cardiac diseases include heart failure, hypertension, rheumatic heart disease, cardiomyopathy, arrhythmias, congenital heart disease, valvular heart disease, aortic aneurysms, peripheral artery disease, thromboembolic disease, and venous thrombosis. Immunocompromised patients are those receiving T-cell immunosuppressants, tumor necrosis factor (TNF) blockers, specific monoclonal antibodies, or corticosteroids at a dose of 0.3 mg/kg/d of prednisone for at least 72 h before the index infection. A critical care stay is considered if the patient is admitted to the Intensive Care Unit (ICU), Cardiac Care Unit (CCU), or Burn Unit (BU) for more than 24 h. Death was considered if the symptomatic patient had a positive *A. baumannii* culture and died before the resolution of signs of *A. baumannii* infection during the same hospitalization. The following criteria demonstrate infection resolution: subsiding of presenting symptoms, normal laboratory values of white blood cells (WBC) and C-reactive protein (CRP), or negative culture of the same sample source as the original index infection.

2.4. Statistical Analysis

Descriptive statistics were used to summarize demographics and patient characteristics. The $\chi^2$ test or Fisher’s exact test was used for categorical data, and the Student’s t-test or Wilcoxon rank-sum test was used for numerical data.

A correlation analysis was performed to investigate the nature and strength of the relationship between risk factors and mortality; $p$ values < 0.05 were considered statistically significant. R software (https://www.r-project.org/) was used for all statistical analyses.

3. Results

Clinical and microbiological data from 321 symptomatic adult inpatients (total patient days 14108) with confirmed *A. baumannii* clinical infections were reviewed as part of an initiative to evaluate variables associated with all-cause (44%), 14-day (12%), and 28-day (13%) infection-related mortality in the context of evidence-based clinical and antimicrobial recommendations. The cumulative number of risk factors was a significant predictor of mortality; every additional risk factor increased all-cause in-hospital mortality rates by a factor of 1.5 ($p < 0.05$, OR: 1.5). The characteristics of the patients, hospitalization and infection-related details are shown in Tables 1–3, respectively.

### Table 1. Patient-related variables versus mortality rates (Binary logistic regression).

|                                | All-Cause in-Hospital Mortality $n = 140$ (44%) | 14-Day Mortality $n = 37$ (12%) | 28-Day Mortality $n = 41$ (13%) |
|--------------------------------|-----------------------------------------------|---------------------------------|---------------------------------|
|                                | No | % | $p$ | OR | CI | No | % | $p$ | OR | CI | No | % | $p$ | OR | CI |
| Age, median (IQR)              | 69 | 60-76 | 0.000 | 1.04 | 1.03-1.06 | 23 | (60-77) | 0.006 | 1.03 | 1.01-1.05 | 68 | (56-76) | 0.020 | 1.02 | 1.00-1.04 |
| Age > 65 years                 | 88 | 62.9% | 0.000 | 3.41 | 2.15-5.42 | 23 | 62.2% | 0.040 | 2.09 | 1.03-4.23 | 25 | 61.0% | 0.044 | 1.99 | 1.02-3.90 |
| Male                           | 93 | 66.4% | 0.001 | 2.14 | 1.35-3.37 | 24 | 64.9% | 0.254 | 1.51 | 0.74-3.09 | 31 | 76.5% | 0.009 | 2.73 | 1.29-5.77 |
| Female                         | 47 | 33.6% | 0.47 | 0.30-0.74 | 13 | 35.1% | 0.66 | 0.32-1.35 | 10 | 24.4% | 0.009 | 0.37 | 0.17-0.78 |
| Any comorbidities              | 126 | 90.0% | 0.000 | 5.29 | 2.82-9.92 | 34 | 91.9% | 0.018 | 4.29 | 1.28-14.37 | 35 | 85.4% | 0.101 | 2.13 | 0.86-5.28 |
| Diabetes                       | 74 | 52.9% | 0.000 | 2.38 | 1.51-3.75 | 19 | 51.4% | 0.182 | 1.60 | 0.80-3.18 | 22 | 53.7% | 0.084 | 1.79 | 0.93-3.46 |
| Chronic renal failure          | 32 | 22.9% | 0.070 | 1.69 | 0.96-2.98 | 10 | 27.0% | 0.153 | 1.78 | 0.81-3.91 | 8 | 19.5% | 0.841 | 1.09 | 0.47-2.50 |
| Active malignancy              | 7 | 5.0% | 0.623 | 1.31 | 0.45-3.82 | 2 | 5.4% | 0.742 | 1.30 | 0.28-6.03 | 1 | 2.4% | 0.526 | 0.51 | 0.07-4.03 |
| Immuno-suppressed              | 4 | 2.9% | 0.959 | 1.04 | 0.27-3.93 | 1 | 2.7% | 0.968 | 0.96 | 0.12-7.89 | 0 | 0.0% | * | * | * |
| Chronic cardiac diseases       | 97 | 69.3% | 0.000 | 2.72 | 1.71-4.33 | 28 | 75.7% | 0.012 | 2.74 | 1.25-6.02 | 27 | 65.9% | 0.166 | 1.62 | 0.82-3.23 |
| HIV follow-up/AIDS            | 1 | 0.7% | 0.855 | 1.30 | 0.08-20.89 | 1 | 2.7% | 0.148 | 7.86 | 0.48-128.43 | 0 | 0.0% | * | * | * |
| Chronic respiratory disease   | 23 | 16.4% | 0.007 | 2.77 | 1.33-5.78 | 6 | 16.2% | 0.275 | 1.70 | 0.66-4.42 | 9 | 22.0% | 0.019 | 2.75 | 1.18-6.38 |

No.: number, $p$: probability value, OR: odds ratio, CI: confidence interval, IQR: intra-quartile range, *: value cannot be produced by software.
Table 2. Hospitalization details versus mortality rates (Binary logistic regression).

| Variable | LOS, median (IQR) | Antibiotics | No. | % | p OR CI | Admission to critical care area | % | p OR CI | Admission with ID diagnosis | % | p OR CI | Admission with a non-ID diagnosis | % | p OR CI |
|----------|-------------------|-------------|-----|---|---------|-------------------------------|---|-------|--------------------------------|---|-------|---------------------------------|---|-------|
| Hospital-acquired infection | 93 | 50.0% | 0.001 | 2.18 | 1.38–3.54 | 12 | 9.3% | 0.039 | 1.39–5.69 | 4 | 7.5% | 0.102 | 1.33–8.15 | 2 | 9.3% | 0.465 | 1.98–10.58 |
| Antibiotic-related ADE | 86 | 61.4% | 0.000 | 2.57 | 1.53–4.27 | 25 | 60.0% | 0.106 | 1.52–9.81 | 10 | 26.3% | 0.165 | 1.21–2.05 | 2 | 9.3% | 0.050 | 1.26–6.72 |

Table 3. Infection-related details versus mortality rates (Binary logistic regression).

| Variable | Blood sample | Patient-related device sample | Respiratory sample | Skin & soft tissue sample | Urine sample | Infection with MDRAB | Infection with sensitive AB | Hospital-acquired infection |
|----------|--------------|------------------------------|-------------------|--------------------------|-------------|----------------------|--------------------------|---------------------------|
| % | 12.0% | 5.8% | 21.2% | 20.5% | 2.2% | 10.7% | 3.9% | 33.6% |
| p | 0.207 | 0.000 | 0.142 | 0.207 | 0.000 | 0.000 | 0.207 | 0.000 |
| CI | 1.98–0.71 | 1.38–2.12 | 12.1–1.69 | 1.46–1.39 | 0.02–0.02 | 0.5–1.55 | 0.29–1.58 | 0.61–0.73 |

No.: number, p: probability value, OR: odds ratio, CI: confidence interval, IQR: intra-quartile range, ID: infectious disease, LOS: length of stay, H/O: history of, *, value cannot be produced by software.
3.1. Patient-Related Risk Factors

Age: The overall study sample’s median (IQR) age was 62.7 (38.9–75.2); for recovered patients, it was 48 (30.9–70.4), and 69.3 (60.6–76.9) for non-survivals. Patients > 65 years had a higher all-cause mortality rate compared to those ≤ 65 years (p = 0.000, OR: 3.41). Age maintains the same effect on 14-day and 28-day mortalities (p = 0.040, OR: 2.09) and (p = 0.044, OR: 1.99), respectively.

Gender: Both sexes were nearly equally represented in the study sample, with 180 (56%) males and 141 (44%) females. High odds ratios of deaths were noticed in males among all-cause and 28-day mortalities (p = 0.001, OR: 2.14) and (p = 0.009, OR: 2.73), respectively.

Comorbid conditions: Compared to patients without comorbidities, the presence of any comorbid condition increased all-cause and 14-day mortality rates by nearly five times (p = 0.000, OR: 5.29) and (p = 0.018, OR: 4.29), respectively. Among all chronic diseases, diabetes mellitus (p = 0.000, OR: 2.38), chronic cardiac (p = 0.000, OR: 2.72), and respiratory (p = 0.007, OR: 2.77) diseases were the most significant predictors of all-cause mortality.

3.2. Hospitalization-Related Risk Factors

Length of stay (LOS): The overall study sample’s median (IQR) LOS was 20 (9.5–40) days; for recovered patients, it was 17 (8–35), and 23 (13–50) for non-survivals. Prolonged hospitalization was found to be a significant predictor for 14-day (p < 0.000, OR: 0.86) and 28-day (p < 0.024, OR: 0.98) mortalities.

Admission to critical care units: Patients admitted to critical care units have a nearly three-fold all-cause mortality rate compared to those admitted to general wards (p = 0.000, OR: 2.86). Meanwhile, it has no statistically significant effect on 14-day and 28-day mortalities.

History of hospitalization: Both a 90-day history of hospitalization and the hospitalization due to chronic disease management were significant predictors of earlier deaths (14-day) (p = 0.024, OR: 2.22) and 28-day (p = 0.046, OR: 1.62).

Antibiotic-related adverse events: ADE were found to be significantly associated with all-cause mortality (p = 0.000, OR: 3.13) and linked to a non-significant high odds ratio of 28-day deaths.

3.3. Infection-Related Risk Factors

Admission diagnosis: When compared to patients admitted with a non-infectious diagnosis, patients with an infectious disease diagnosis had significantly higher rates of all-cause (p = 0.000, OR: 3.12), 14-day (p < 0.006, OR: 2.98), and 28-day (p < 0.01, OR: 2.61) mortality.

Site of infection: Patients with pneumonia had significantly higher all-cause in-hospital mortality rates (p = 0.000, OR: 2.85) than other types of infections, while bacteremic patients died earlier (28-day) (p = 0.042, OR: 2.83).

MDR-related infections: Patients infected with MDRAB had a significantly higher all-cause mortality rate than those infected with sensitive strains (p = 0.000, OR: 3.43). However, this effect completely vanished with the near-term deaths.

Hospital-acquired infections: Hospital-acquired A. baumannii infections significantly increase all-cause in-hospital mortality (p = 0.027, OR: 1.68) but do not affect other mortalities.

Exposure to infections: A 90-day previous exposure to any bacterial infection (p < 0.050, OR: 2.05), particularly Gram-negative bacteria (p = 0.026, OR: 2.31) (most notably P. aeruginosa (p = 0.039, OR: 2.65) and E. coli (p = 0.039, OR: 2.86), was associated with highly significant odd ratios of early-onset (14-day) deaths.

Concurrent polymicrobial infections: When compared to pure A. baumannii infection, late-onset (all-cause) mortality rates were significantly higher in the presence of concurrent infections (p = 0.000, OR: 2.66), most likely in concurrent infection with K. pneumonia (p = 0.001, OR: 2.18), P. aeruginosa (p = 0.022, OR: 1.70), and other Gram-negative isolates (p = 0.000, OR: 2.57).
4. Discussion

This research examined 17 variables that were thought to contribute to *A. baumannii* infection-related mortality in hospitalized patients. Binary logistic regression analyses were used. Our findings are discussed as modifiable and non-modifiable risk factors to guide targeted clinical interventions to reduce infection-related mortality in the early and late onsets.

4.1. Modifiable Risk Factors

Prolonged hospitalization session was a significant predictor of mortality rates; patients admitted for >7 days were more likely to die than those admitted for less than 7 days ($p < 0.05$). Among the 259 patients who stayed for > 7 days, 169 (65%) acquired MDRAB infection, significantly contributing to early-onset mortality. While Thorne was unable to link LOS to *A. baumannii*-related acquisition or mortality [15], others have linked LOS to infections and mortality caused by a variety of resistant pathogens such as (methicillin-resistant *S. aureus*, extended-spectrum β-lactamase-producing *K. pneumoniae*, and carbapenem-resistant *A. baumannii*) [16]. Thus, early discharge and home treatment may reduce infection acquisition and treatment-related costs. The antimicrobial stewardship team can promote early discharge strategies by reviewing patient isolation protocols, optimizing surgical prophylaxis protocols, and switching IV to PO whenever possible [17].

Admission to critical care units (92/321) was associated with a non-significant high odds ratio of early-onset mortality while significantly contributing to a higher all-cause mortality rate than general wards ($p < 0.05$). This may be due to excessive catheterization or lax infection control measures in these areas, which may have resulted in its closure to allow disinfection [18]. Many studies support our findings; Choe and colleagues discovered that prior ICU admission significantly contributed to 30-day mortality due to *A. baumannii* ($p = 0.04$) [19]. Meanwhile, Niu and colleagues discovered that ICU stay is a risk factor for 28-day mortality ($p = 0.04$). In an American study, Blanco discovered that patients positive for *A. baumannii* at ICU admission were 15.2 times more likely to develop a subsequent positive clinical culture for *A. baumannii* and 1.4 times more likely to die during the current hospitalization ($p = 0.01$) [20]. In a prospective surveillance study done by Ganesan and colleagues, CRAB ranks second after *K. pneumoniae* as one of the main causative pathogens for device-associated hospital-acquired infections in patients admitted to critical care areas [21].

Intuitively, patients admitted to critical care areas usually suffer a diminished health status, weakened immunity, and are more vulnerable to invasive maneuvers and highly virulent pathogens, necessitating regular disinfection of the ICU environment and equipment, as well as optimal intubation practice with the goal of avoiding excessive catheterization [22].

Hospital-acquired infections (HAIs) significantly contribute to all-cause mortality with a non-significant high odds ratio of 28-day mortality. Similarly, hospitals in the United States and Thailand noticed that mortality rates for patients with bloodstream infections (BSIs) caused by community-acquired *A. baumannii* were significantly lower than those for patients with hospital-acquired *A. baumannii* [23,24]. This could be explained by the higher prevalence of virulent phenotypes of *A. baumannii* in hospitals due to increased antimicrobial treatment exposure. Adopting better multidisciplinary infection control practices, regular disinfection of patient care equipment, reducing unnecessary admissions through updated outpatient practices, and increasing outpatient care resources contribute to reduced HAIs [22].

Concurrent polymicrobial infections were a statistically significant predictor of late-onset mortality ($p < 0.05$), most likely in patients infected with *Klebsiella pneumonia, Pseudomonas aeruginosa*, and other Gram-negative isolates. The ability of *K. pneumoniae, P. aeruginosa*, and other Gram-negative isolates to disseminate resistance determinants via horizontal gene transfer (HGT) to *A. baumannii* strains may explain the high prevalence of MDRAB infections in patients with polymicrobial infections (210/239, 88%). Yung and colleagues did not replicate this finding; they found no significant difference in 14-day mortality.
among patients with monomicrobial and polymicrobial *A. baumannii* BSIs (26.9% vs. 29.2%, \( p < 0.77 \)), with relatively higher rates observed in polymicrobial BSIs with concomitant isolation of *E. coli*, *P. aeruginosa*, and *Enterobacter* spp. \[25\]. Better identification and monitoring of HGT pathways, robust infection control practices, and regular disinfection of healthcare areas contribute to the limited intra-species spread of resistance determinants \[26\].

Antibiotic-related adverse events (ADE) were found to be significantly associated with all-cause mortality \( (p < 0.000) \) and to have a non-significantly high odds ratio of 28-day deaths. Patients \( (147/321, 46\%) \) experienced adverse events due to prolonged antibiotic use; more likely, 92% fungal infection, 6% acute renal failure, and 2% other adverse events. Moreover, ADR development was associated with a longer LOS median (IQR) of 26 (15–71) compared to 16 (7–31), \( (p < 0.05) \), in patients who did not develop ADR. Dose and duration optimization, de-escalation of antimicrobial treatment, and therapeutic drug monitoring remain effective tactics to minimize adverse drug reactions \[27,28\].

### 4.2. Non-Modifiable Risk Factors

Age maintains a significant directly proportional effect on early-onset and late-onset mortality; patients >65 years had higher mortality rates compared to those ≤65 years, which coincides with a Chinese study that concluded hospital-acquired *A. baumannii* infections in patients aged >65 years were found to be a high-risk predictor of mortality \[29\].

Males showed statistically significant high odd ratios of all-cause and 28-day mortalities, which is consistent with a multicentered study by many Serbian hospitals \[30\]. In this study, the correlation of mortality rates with males can be explained by several statistically associated variables, such as the need for critical care unit admission \( (p = 0.02) \), the acquisition of MDR-related infections \( (p = 0.001) \), and exposure to polymicrobial infections \( (p = 0.000) \).

Underlying chronic comorbidities were significant risk factors for mortality \( (p < 0.000) \). Our findings are consistent with those of Chang and colleagues, who identified illness severity, duration of mechanical ventilation, prior hospitalization, and underlying conditions as predictors of mortality \[31\]. It also matches the finding of a recent (2019) Chinese meta-analysis that linked comorbidities to mortality caused by *A. baumannii* infections \[32\]. Others concluded that underlying illnesses are more influential than the infection itself as a cause of death \[33\], implying that concurrent comorbidities to *A. baumannii* infections must be clinically stabilized as soon as possible to improve outcomes. Among all chronic diseases, diabetes mellitus \( (p < 0.05) \), chronic cardiac \( (p < 0.05) \), and respiratory \( (p < 0.05) \) diseases were the most significant predictors of all-cause mortality.

MDR-related infections were associated with a significantly higher all-cause mortality rate than those infected with sensitive strains \( (p < 0.05, OR: 3.43) \). However, it was still associated with non-significant high odds ratio of near-term deaths. Patients with MDRAB infections had a high incidence of polymicrobial infections (88%) and chronic comorbidities (66%); these were likely the confounders contributing to increased mortality. Our finding matches many studies from different parts of the world; they found several folds increase in mortality rate in MDRAB infected patients than in those infected with susceptible phenotypes, as well as increased hospital and intensive care unit length of stay \[34–36\].

Patients who presented on admission with an infectious disease diagnosis had significantly higher mortality rates of all types. Patients with pneumonia, in particular, had the highest mortality rates of any infection; meanwhile, bacteremic patients died earlier. The high mortality rates among respiratory and BSIs can be explained by excessive intubation and catheterization, particularly in critical care areas, which may serve as a reservoir for resistant phenotypes; the high incidence of MDRAB infections among both groups (respiratory and bacteremia patients); (85%) and (82%), respectively explains mounted deaths. A high death rate was reported in France due to case severity and limited antibiotic options against MDRAB respiratory and bloodstream infections. \[37\].

History of hospitalization—primarily due to a chronic condition—and exposure to infection were highly significant predictors of early-onset mortality. Exposure to bacterial
infection, particularly *P. aeruginosa* and *E. coli*, were associated with significantly high odds of early-onset (14-day) deaths. Many studies linked morbidity and mortality risks to previous healthcare exposure [38,39], which is an alarming sign to adopt a firm infection control policy.

History of infection with *P. aeruginosa* and *E. coli* contributed significantly to early onset mortality which may be due to disseminated resistance determinants to current isolates. Further studies are needed to assess the impact of prior exposure to certain bacterial strains that may serve as a source of transferrable resistance determinants and the exposure to potentially high resistance-inducing antimicrobials. Identifying these factors may help identify patients at high risk for MDRAB infection-related mortality and place extra emphasis on early intervention. It would also be conducive in any endeavors aiming to construct an algorithm for early detection and prompt treatment of high-risk patient groups.

While we incorporated numerous possible risk factors in our analysis, a limitation to our study could be that the characteristics of the cohort studied might not be generalizable to other geographic locations, and consideration of our findings in conjunction with other similar studies could consolidate the construction of a robust model to predict and mitigate risk factors for mortality.

5. Conclusions

Old age, prolonged hospitalization, inadequate infection control, resorting to invasive procedures, host health status, and antibiotic overuse appear to be the most important risk factors for nosocomial infection-related mortality. Nosocomial infections are avoidable if we improve the operation of healthcare services based on multidisciplinary infection control practice, regular disinfection of patient care equipment, and bedside antiseptic dispensers with instructions to remind staff to clean their hands.

Improved outcomes may result from better intubation practice, shorter hospital stays, prompt medical stabilization of comorbidities, and limiting unnecessary admissions to critical care areas. The antimicrobial stewardship team can promote early discharge and minimize HAI exposure through optimal antibiotic selection and de-escalation, optimized surgical prophylaxis protocols, and IV to PO switching tactics whenever possible. More research is needed to investigate the effect of antibiotics on the dynamics of *A. baumannii* microbial resistance in relation to multidrug-resistant outbreaks.

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References

1. Sepute, V.; Povilonis, J.; Sutiedeliene, E. Novel variants of AbaR resistance islands with a common backbone in Acinetobacter baumannii isolates of European clone II. *Antimicrob. Agents Chemother.* 2012, 56, 1969–1973. [CrossRef] [PubMed]

2. Gordon, N.C.; Wareham, D.W. Multidrug-resistant Acinetobacter baumannii: Mechanisms of virulence and resistance. *Int. J. Antimicrob. Agents* 2010, 35, 219–226. [CrossRef] [PubMed]

3. Wisplinghoff, H.; Edmond, M.B.; Pfaffer, M.A.; Jones, R.N.; Wenzel, R.P.; Seifert, H. Nosocomial bloodstream infections caused by Acinetobacter species in United States hospitals: Clinical features, molecular epidemiology, and antimicrobial susceptibility. *Clin. Infect. Dis.* 2003, 31, 690–697. [CrossRef] [PubMed]

4. Ceylan, B.; Arslan, F.; Sipahi, O.R.; Sunbul, M.; Ormen, B.; Hakyemez, I.N.; Turunc, T.; Yildiz, Y.; Karsen, H.; Karagoz, G.; et al. Variables determining mortality in patients with Acinetobacter baumannii meningitis/ventriculitis treated with intrathecal colistin. *Clin. Neurol. Neurosurg.* 2017, 153, 43–49. [CrossRef] [PubMed]

5. Balkhair, A.; Al-Muharrmi, Z.; Al’Adawi, B.; Al Busaiedi, I.; Taher, H.B.; Al-Siyabi, T.; Al Amin, M.; Hassan, K.S. Prevalence and 30-day all-cause mortality of carbapenem and colistin resistant bacteraemias caused by Acinetobacter baumannii, Pseudomonas aeruginosa, and Klebsiella pneumoniae: A description of a decade long trend. *Int. J. Infect. Dis.* 2019, 85, 10–15. [CrossRef] [PubMed]

6. Tacconelli, E.; Carrara, E.; Savoldi, A.; Harbarth, S.; Mendelson, M.; Monnet, D.L.; Pulcini, C.; Kahlmeter, G.; Kluytmans, J.; Carmeli, Y.; et al. Discovery, research, and development of new antibiotics: The WHO priority list of antibiotic-resistant bacteria and tuberculosis. *Lancet Infect. Dis.* 2018, 18, 318–327. [CrossRef]

7. Rice, L.B. Federal funding for the study of antimicrobial resistance in nosocomial pathogens: No ESKAPE. *J. Infect. Dis.* 2008, 197, 1079–1081. [CrossRef]

8. Centers for Disease Control and Prevention. Antibiotic Resistance Threats in the United States, 2013. CDC Website. 16 September 2013. Available online: www.cdc.gov/drugsusceptibility/threatreport-2013 (accessed on 30 November 2013).

9. Hidron, A.I.; Edwards, J.R.; Patel, J.; Horan, T.C.; Sievert, D.M.; Pollock, D.A.; Fridkin, S.K. NHSN annual update: Antimicrobial-resistant pathogens associated with healthcare-associated infections: Annual summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2006–2007. *Infect. Control Hosp. Epidemiol.* 2008, 29, 996–1011. [CrossRef] [PubMed]

10. Fu, Q.; Ye, H.; Liu, S. Risk factors for extensive drug-resistance and mortality in geriatric inpatients with bacteremia caused by Acinetobacter baumannii. *Am. J. Infect. Control* 2015, 43, 857–860. [CrossRef]

11. Freire, M.P.; de Oliveira Garcia, D.; Garcia, C.P.; Campagnari Bueno, M.F.; Camargo, C.H.; Kono Magri, A.S.G.; Francisco, G.R.; Reginhini, R.; Vieira, M.F.; Ibrahim, K.Y.; et al. Bloodstream infection caused by extensively drug-resistant Acinetobacter baumannii in cancer patients: High mortality associated with delayed treatment rather than with the degree of neutropenia. *Clin. Microbiol. Infect.* 2016, 22, 352–358. [CrossRef]

12. 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–e815. [CrossRef] [PubMed]

13. Alrahmany, D.; Omar, A.F.; Harb, G.; El Nekidy, W.S.; Ghazi, I.M. Acinetobacter baumannii Infections in Hospitalized Patients, Treatment Outcomes. *Antibiotics* 2021, 10, 630. [CrossRef] [PubMed]

14. Clinical and Laboratory Standards Institute. Standards Development Policies and Process October 2013. Available online: https://www.cdc.gov/drugsusceptibility/clsi-standards.html (accessed on 15 June 2022).

15. Thorne, A.; Luo, T.; Durairajan, N.K.; Kaye, K.; Foxman, B. Risk factors for endemic Acinetobacter Baumannii colonization: A case-case study. *Am. J. Infect. Control* 2019, 47, 1294–1297. [CrossRef]

16. The cost of antibiotic resistance: Effect of resistance among Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, and Pseudomonas aeruginosa on length of hospital stay. *Infect. Control Hosp. Epidemiol.* 2002, 23, 106–108. [CrossRef] [PubMed]

17. World Health Organization. *Prevention of Hospital-Acquired Infections: A Practical Guide*; World Health Organization: Geneva, Switzerland, 2002.

18. Zanetti, G.; Blanc, D.S.; Federli, I.; Raffoul, W.; Petignat, C.; Maravic, P.; Francioli, P.; Berger, M.M. Importation of Acinetobacter baumannii into a burn unit: A recurrent outbreak of infection associated with widespread environmental contamination. *Infect. Control Hosp. Epidemiol.* 2007, 28, 723–725. [CrossRef] [PubMed]

19. Choe, Y.J.; Lee, H.J.; Choi, E.H. Risk Factors for Mortality in Children with Acinetobacter baumannii Bacteremia in South Korea: The Role of Carbapenem Resistance. *Microb. Drug Resist.* 2019, 25, 1210–1218. [CrossRef]

20. Blanco, N.; Harris, A.D.; Rock, C.; Johnson, K.; Pineles, L.; Bonomo, R.A.; Srinivasan, A.; Pettigrew, M.M.; Thom, K.A.; the CDCEP. Risk Factors and Outcomes Associated with Multidrug-Resistant Acinetobacter baumannii upon Intensive Care Unit Admission. *Antimicrob. Agents Chemother.* 2018, 62, e01631-17. [CrossRef]

21. Ganesan, V.; Sundaramurthy, R.; Sr; Thiruvananmalai, R.; Sivakumar, V.A.; Udayasankar, S.; Arunagiri, R.; Charles, J.; Chavan, S.K.; Balan, Y.; Sakthivadivel, V. Device-Associated Hospital-Acquired Infections: Does Active Surveillance with Bundle Case Offer a Pathway to Minimize Them? *Cureus* 2021, 13, e19331. [CrossRef]

22. Mehta, Y.; Gupta, A.; Todi, S.; Myatra, S.; Samaddar, D.P.; Patil, V.; Bhattacharyya, P.K.; Ramesubban, S. Guidelines for prevention of hospital acquired infections. *Indian J. Crit. Care Med.* 2018, 14, 149–163. [CrossRef] [PubMed]

23. Ellis, D.; Cohen, B.; Liu, J.; Larson, E. Risk factors for hospital-acquired antimicrobial-resistant infection caused by Acinetobacter baumannii. *Antimicrob. Resist. Infect. Control* 2015, 4, 40. [CrossRef] [PubMed]
24. Chusri, S.; Chongsuvivatwong, V.; Silpapojakul, K.; Singkhaman, K.; Hortiwakul, T.; Charernmak, B.; Doi, Y. Clinical characteristics and outcomes of community and hospital-acquired Acinetobacter baumannii bacteremia. *J. Microbiol. Immunol. Infect.* 2019, 52, 796–806. [CrossRef] [PubMed]

25. Wang, Y.-C.; Ku, W.-W.; Yang, Y.-S.; Kao, C.-C.; Kang, F.-Y.; Kuo, S.-C.; Chiu, C.-H.; Chen, T.-L.; Wang, F.-D.; Lee; et al. Is Polymicrobial Bacteremia an Independent Risk Factor for Mortality in Acinetobacter baumannii Bacteremia? *J. Clin. Med.* 2020, 9, 153. [CrossRef] [PubMed]

26. Wyres, K.L.; Holt, K.E. Klebsiella pneumoniae as a key trafficker of drug resistance genes from environmental to clinically important bacteria. *Curr. Opin. Microbiol.* 2018, 45, 131–139. [CrossRef] [PubMed]

27. Shamna, M.; Dilip, C.; Ajmal, M.; Linu Mohan, P.; Shinu, C.; Jaler, C.P.; Mohammed, Y. A prospective study on Adverse Drug Reactions of antibiotics in a tertiary care hospital. *Saudi Pharm. J.* 2014, 22, 303–308. [CrossRef] [PubMed]

28. Jung, I.Y.; Kim, J.J.; Lee, S.J.; Kim, J.; Seong, H.; Jeong, W.; Choi, H.; Jeong, S.J.; Ku, N.S.; Han, S.H.; et al. Antibiotic-Related Adverse Drug Reactions at a Tertiary Care Hospital in South Korea. *BioMed Res. Int.* 2017, 2017, 4304973. [CrossRef] [PubMed]

29. Zhou, Q.; Fan, L.; Tai, X.; Tan, L.; Zhang, X. Estimating extra length of stay and risk factors of mortality attributable to healthcare-associated infection at a Chinese university hospital: A multi-state model. *BMC Infect. Dis.* 2019, 19, 975. [CrossRef]

30. Djordjevic, Z.M.; Folic, M.M.; Folic, N.D.; Gajovic, N.; Gajovic, O.; Jankovic, S.M. Risk factors for hospital infections caused by carbapenem-resistant Acinetobacter baumannii. *J. Infect. Dev. Ctries.* 2016, 10, 1073–1080. [CrossRef]

31. Liu, C.-P.; Shih, S.-C.; Wang, N.-Y.; Wu, A.Y.; Sun, F.-J.; Chow, S.-F.; Chen, T.-L.; Yan, T.-R. Risk factors of mortality in patients with carbapenem-resistant Acinetobacter baumannii bacteremia. *J. Microbiol. Immunol. Infect.* 2016, 49, 934–940. [CrossRef]

32. Du, X.; Xu, X.; Yao, J.; Deng, K.; Chen, S.; Shen, Z.; Yang, L.; Feng, G. Predictors of mortality in patients infected with carbapenem-resistant Acinetobacter baumannii: A systematic review and meta-analysis. *Am. J. Infect. Control* 2019, 47, 1140–1145. [CrossRef]

33. Jang, T.N.; Lee, S.H.; Huang, C.H.; Lee, C.L.; Chen, W.Y. Risk factors and impact of nosocomial Acinetobacter baumannii bloodstream infections in the adult intensive care unit: A case-control study. *J. Hosp. Infect.* 2009, 73, 143–150. [CrossRef]

34. Kumar, V.; Gupta, N.; Vaish, V.B.; Gupta, S. Distribution trends & antibiogram pattern of Salmonella enterica serovar Newport in India. *Indian J. Med. Res.* 2016, 144, 82–86. [PubMed]

35. Wisplinghoff, H.; Perbix, W.; Seifert, H. Risk factors for nosocomial bloodstream infections due to Acinetobacter baumannii: A case-control study of adult burn patients. *Clin. Infect. Dis.* 1999, 28, 59–66. [CrossRef] [PubMed]

36. Sunenshine, R.H.; Wright, M.O.; Maragakis, L.L.; Harris, A.D.; Song, X.; Hebben, J.; Cosgrove, S.E.; Anderson, A.; Carnell, J.; Jernigan, D.B.; et al. Multidrug-resistant Acinetobacter infection mortality rate and length of hospitalization. *Emerg. Infect. Dis.* 2007, 13, 97–103. [CrossRef] [PubMed]

37. Munier, A.L.; Biard, L.; Legrand, M.; Rousseau, C.; Lafaurie, M.; Donay, J.L.; Flicoteaux, R.; Mebazaa, A.; Mimoun, M.; Molina, J.M. Incidence, risk factors and outcome of multi-drug resistant Acinetobacter baumannii nosocomial infections during an outbreak in a burn unit. *Int. J. Infect. Dis.* 2019, 79, 179–184. [CrossRef] [PubMed]

38. Cohen, B.; Liu, J.; Cohen, A.R.; Larson, E. Association between Healthcare-Associated Infection and Exposure to Hospital Roommates and Previous Bed Occupants with the Same Organism. *Infect. Control Hosp. Epidemiol.* 2018, 39, 541–546. [CrossRef]

39. Garnacho-Montero, J.; Ortiz-Leyba, C.; Fernandez-Hinojosa, E.; Aldabo-Pallas, T.; Cayuela, A.; Marquez-Vacaro, J.A.; Garcia-Curiel, A.; Jimenez-Jimenez, F.J. Acinetobacter baumannii ventilator-associated pneumonia: Epidemiological and clinical findings. *Intensive Care Med.* 2005, 31, 649–655. [CrossRef]