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# Epidemiological and Clinical Insights into Acinetobacter baumannii: A Six-Year Study on Age, Antibiotics, and Specimens

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**Background:** This six-year retrospective study provides an in-depth analysis of the epidemiological and clinical patterns associated with *Acinetobacter baumannii* (*A. baumannii*) infections, focusing on age distribution, antibiotic resistance profiles, and specimen types.

**Aim:** The research examines the incidence and characteristics of *both* non-Multi-Drug Resistant (non-MDR) and Multi-Drug Resistant (MDR) *A. baumannii* strains by reviewing patient records from January 2016 to December 2022.

**Methods:** Through a statistical analysis, the study highlights the incidence rates across diverse age groups and explores the impact of antibiotic treatment regimens on infection outcomes. Additionally, it identifies the primary clinical specimen types for each strain, noting an association between non-MDR *A. baumannii* and midstream urine samples, while MDR *A. baumannii* strains were more frequently found in respiratory, wound, peripheral, and central line swaps/specimens.

**Results:** The results indicate that in 2016, non-MDR *A. baumannii* infections were notably more frequent compared to MDR *A. baumannii* cases. However, a significant shift occurred in 2021 and 2022, with a marked decrease in non-MDR *A. baumannii* cases and an increase in MDR *A. baumannii* infections. Antibiotic susceptibility testing revealed that non-MDR strains were commonly tested against cefazolin, ceftazidime, ciprofloxacin, gentamicin, nitrofurantoin, oxacillin, piperacillin/tazobactam, and trimethoprim/sulfamethoxazole. In contrast, MDR strains were frequently tested against amikacin, cefepime, colistin, meropenem, imipenem, and tigecycline.

**Conclusion:** This study enhances the understanding of *A. baumannii* clinical behaviour and resistance patterns, offering valuable insights to support future research and inform strategies for infectious disease management and control.

Keywords: Acinetobacter baumannii, MDR, the epidemiological and clinical patterns

## Introduction

*A. baumannii*, a resilient and opportunistic Gram-negative bacterium, has emerged as a significant healthcare-associated pathogen, posing formidable challenges in clinical settings worldwide.<sup>1,2</sup> Recognized as one of the most formidable multidrug-resistant bacteria, it contributes to approximately 7300 infection cases and 500 fatalities annually.<sup>3</sup> Its impact on public health is amplified by the limited availability of effective antibiotic treatments and diagnostic methods to address its associated risks.<sup>3</sup> As one of the ESKAPE pathogens, *A. baumannii* is a primary contributor to MDR and extensively drug-resistant (XDR) healthcare-associated infections globally.<sup>4</sup>

*Acinetobacter* can endure on dry surfaces for extending periods, challenging hospital infection control measures and positioning it as a serious nosocomial threat with the potential to significantly impact healthcare systems on a wider scale.<sup>5</sup> While commonly encountered in healthcare settings, initial infections may originate from individuals entering from external facilities. Its ability to develop resistance to multiple antimicrobial agents, coupled with its capacity for prolonged survival on environmental surfaces, underscores its role as a leading cause of nosocomial infections.<sup>5,6</sup>

Over the past few decades, *A. baumannii* has become a notable cause of healthcare-acquired infections, including pneumonia, bloodstream infections, wound infections, and urinary tract infections.<sup>7</sup> Effective control of *A. baumannii* requires a comprehensive understanding of its epidemiology, virulence factors, and antimicrobial resistance mechanisms to mitigate its impact on patient outcomes.<sup>6,7</sup> A significant rise in nosocomial infections has been linked to the emergence of *A. baumannii* strains that exhibit resistance to a broad spectrum of antibiotics, particularly carbapenems, which complicates treatment options. The increase in nosocomial infections has been linked to the spread of *A. baumannii* pathogens, particularly concerning the emergence of strains that resist a broad spectrum of antibiotics, including carbapenems.<sup>7</sup> These antibiotics were once regarded as the primary therapeutic option for combating infections attributed to *A. baumannii*. However, the evolution of resistance mechanisms within *A. baumannii* strains has significantly compromised the efficacy of carbapenems, posing a considerable challenge in managing and treating infections caused by this pathogen.<sup>8,9</sup>

The escalating trend of concurrent resistance to multiple antibiotics has elicited significant concern, particularly in several European nations. By the year 2018, resistance rates had surged above the ominous threshold of 50% in various countries, including Croatia at a staggering 90%, Greece at 80%, Italy at 75%, and Poland at 60%.<sup>10</sup> In the past decade, mortality rates from *A. baumannii* infections have risen significantly across regions, ranging between 30% and 75%. Furthermore, multidrug-resistant *A. baumannii* has emerged as a major threat due to its resistance to multiple antibiotic classes, especially carbapenems and third-generation cephalosporins.<sup>11</sup>

Studies indicate that mortality and disability rates from *A. baumannii* infections are on the rise. Retrospective analyses report mortality rates from these infections ranging from 22.8% to 49.6% in the United States and from 29% to 71.6% in Europe. Mortality associated with *A. baumannii*-related hospital-acquired and ventilator-associated pneumonia was especially high in regions like Western Asia (56.2%), Southern Europe (55.7%), and Northern Africa (53.3%). Within the Mediterranean region, countries such as Greece (68.2%), Turkey (61.4%), and Egypt (53.3%) reported some of the highest mortality rates.<sup>12</sup> In Germany, this pathogen is widespread, with community and hospital-based outbreaks documented in 13 of the country's 16 federal states.<sup>13</sup> In contrast, countries like the United Kingdom, Belgium, and Germany, report comparatively lower rates of antibiotic resistance. However, in the United States, *Acinetobacter* represents a significant public health concern, contributing to an estimated 2% of all Hospital-Acquired Infections (HAIs) identified in 2013. Among these cases, approximately 63% were linked to multi-drug-resistant strains of *A. baumannii*.

*A. baumannii* infections pose a significant burden on healthcare systems and patient outcomes, with an estimated 12,000 cases reported annually.<sup>10,11</sup> Globally, infection rates in intensive care units (ICUs) illustrate the pervasive nature of *A. baumannii*, reaching 14.8% in Africa and 19.2% in Asia.<sup>12,13</sup> In Saudi Arabia, the emergence of MDR *A. baumannii* has raised concerns due to its impact on healthcare delivery and resource allocation.<sup>14</sup>

Certain risk factors, such as prior prolonged antimicrobial therapy, mechanical ventilation, lengthy hospital stays, and severe underlying conditions, contribute to the susceptibility of individuals to MDR *A. baumannii* infections. Chronic conditions such as diabetes mellitus, cancer, renal impairment, and pulmonary disorders further increase the risk,

especially in ICU patients undergoing extended mechanical ventilation.<sup>14,15</sup> In Saudi Arabia, numerous investigations have aimed to uncover potential risk factors associated with *A. baumannii* infections. Findings suggest that endemic strains of *A. baumannii* can disseminate to tracheal secretions in mechanically ventilated patients, particularly among individuals aged 60 and above undergoing prolonged oxygen therapy, increasing the risk of ventilator-associated pneumonia.<sup>14-16</sup>

Furthermore, colonization of the intestinal tract by *A. baumannii* in hospitalized patients has been identified as a potential risk factor for antibiotic resistance and outbreaks of severe infections such as pneumonia and renal disease, with previous studies revealing that 36% of the infected patients had underlying illnesses and 11% were diabetic.<sup>14–16</sup> Identifying these factors could help to find suitable therapeutic targets, potentially leading to advances in the treatment and improved outcomes of infections attributable to this bacterium.<sup>17</sup> To the best of our current knowledge, this study represents a pioneering effort aimed at comprehensively evaluating the incidence, clinical manifestations, associated risk factors, and outcomes of MDR or non-MDR *A. baumannii* infections over an extensive period spanning six years, commencing from January 2016 and concluding in December 2022, among patients receiving care at King Abdulaziz University Hospital.

## Methods

## Study Design and Sample Collection

This retrospective observational study was conducted at King Abdulaziz University Hospital (KAUH), Jeddah, Saudi Arabia, using a record review approach to analyze *A. baumannii* data from the microbiology database. The study included three main phases: sample collection, microbial identification, and data analysis. Data from January 2016 to December 2022 were reviewed, focusing on patient age distributions for MDR and non-MDR *A. baumannii* infections, as well as the annual incidence and sample types most frequently associated with *A. baumannii*. Ethical approval was obtained from the Local Research Ethics Committee at King Abdulaziz University (approval number HA-02-J-008), and it was conducted in full accordance with the principles outlined in the Declaration of Helsinki, which sets ethical standards for research involving human participants. This study utilized anonymized patient data, including age, year of infection, and antibiotic susceptibility profiles, without any personally identifiable information. Given the fully anonymized nature of the data, individual patient consent was not required, in accordance with ethical standards, ensuring the privacy and confidentiality of patient information throughout the study. Microbial identification was conducted according to standard laboratory procedures, including culture on Enriched and selective agar media and incubation under appropriate conditions.

## Microbial Identification of the Acinetobacter baumannii Isolates

Patient samples were cultured on various agar mediums, including 5% sheep blood agar and Columbia blood agar, all sourced from Saudi Prepared Media Laboratories in Riyadh, Saudi Arabia. MacConkey agar plates were placed in a standard incubator at 35–37°C for 18–24 hours. Aerobic and anaerobic blood culture bottles were processed at the Clinical Microbiology Laboratory at King Abdulaziz University Hospital using the BacT/Alert Virtuo microbial detection system, incubating until a positive signal or a maximum of five days. Positive blood culture bottle samples underwent further processing through Gram staining and methylene blue staining. Following the incubation period, *A. baumannii* colonies were identified using the VITEK 2 and VITEK MS MALDI-TOF systems (BioMérieux, Marcy-L'Étoile, France), while the antibiotic sensitivity was obtained usingVITK2 following the manufacturer's instructions.<sup>18,19</sup> Both VITEK 2 and MALDI-TOF were used for colony identification, each with its own strengths and limitations. Generally, both methods yielded consistent results for identifying *A. baumannii*; however, MALDI-TOF provided faster and more specific identification, especially useful for differentiating closely related species. VITEK 2, while reliable, is more prone to occasional misidentifications with rare strains due to its reliance on biochemical profiling rather than mass spectrometry.<sup>16</sup>

#### Statistical Data Analysis

The figures were created, and data analysis was carried out using R version 4.4.0 software. The difference in age distribution between non-MDR and MDR strains was evaluated using the Wilcoxon test. The significant threshold is set at P < 0.05. Categorical data were analysed using the Chi-squared test, and the residual count of (-2,2) was considered significant. It's important to note that for the application of the Chi-squared test, one sample per patient was used to ensure the statistical validity of the test results by maintaining the independence of each data point. As a result, the number of cases recorded each year, the types of specimens collected, and the range of antibiotics analysed were necessarily restricted due to the focused nature of our study on *A. baumannii* infections within a specific patient population at a single institution.

#### Results

This study analysed the records of 1426 unique patients, some of whom were infected more than once or had multiple samples collected during their treatment. The analysis included a total of 2558 cases, with 1141 cases (44.6%) of infections caused by non-MDR *A. baumannii* and 1417 cases (55.4%) of infections caused by MDR *A. baumannii*, from January 2016 to December 2022. To investigate if there was a significant difference in the median ages of patients infected by the two bacterial strains, and to minimize age-related bias, we selected a random sample from the dataset and conducted a Wilcoxon test. The results showed a statistically significant difference in median age, with a P-value of less than 0.0001. The median age was 35 years for the non-MDR strain and 61 years for the MDR strain (Figure 1).

As shown in Figure 2 individuals aged 70–74 years had the highest occurrence of MDR *A. baumannii* infections. Additionally, there was an upward trend in cases observed among individuals between the ages of 30 and 39, and a notable surge in cases was also observed among those aged 50 to 59. This pattern indicates that those in their middle age are the most impacted. Although the incidence of these illnesses declines in older age groups, it nevertheless stays somewhat elevated in comparison to younger groups. For non-MDR *A. baumannii*, a notable incidence was observed in pediatric patients. The occurrence then sharply declines in the 10–19 age group and gradually rises again, with another peak at ages 50–59. This pattern mirrors that of MDR infections although with fewer cases in each age group overall (Figure 2).

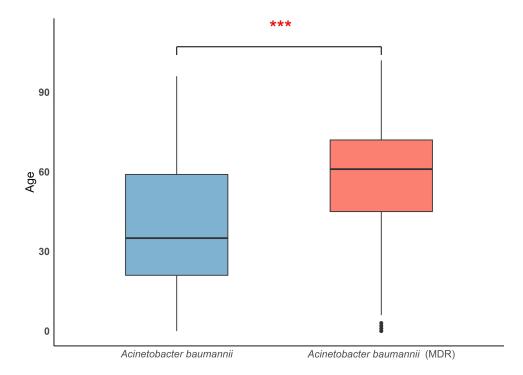


Figure I The age distribution of A. baumannii infections: non-MDR strains (blue) and MDR strains (red), and the P value \*\*\*P <0.001.

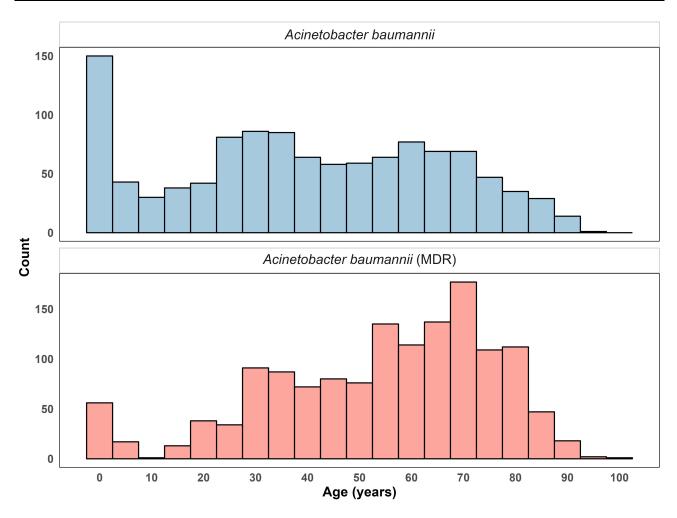


Figure 2 Comparative age distribution of patients with A. baumannii infections non-MDR (blue) and MDR A. baumannii infections (red) between 2016 and 2022. The y-axis shows the number of cases, and the X-axis shows the number of years.

The incidence difference between non-MDR *A. baumannii* and MDR *A. baumannii* from 2016 to 2022 was evaluated using a Chi-square test. The outcomes revealed a P-value <0.0001, indicating a significant difference between the counts of both bacterial strains over this period. To identify which year contributed to this significance, the residual count from the Chi-square test was used. The results show that in 2016, non-MDR *A. baumannii* cases were significantly increased compared to MDR *A. baumannii* cases (Figure 3). However, there was no significant difference between the two strains from 2017 to 2019 (Figure 3). Contrariwise, in 2020 and 2021, MDR *A. baumannii* increased significantly compared to non-MDR *A. baumannii* (Figure 3). This increase was surprising due to the fact that in 2020, more enhanced measures were applied in hospitals and clinical settings to cope with the spread of coronavirus disease 2019 (COVID-19) (Figure 3). By 2022, the counts for both bacterial strains remained at similar infection rates.

Specimens collected from *A. baumannii* strains originated from different infection sites within patients, indicating that each bacterial strain may have a distinct site of preference for infection. To examine whether certain bacterial strains were more commonly associated with specific specimen types, a Chi-squared test was applied to evaluate the relationship between the type of bacterial strain and the type of specimen collected. The results indicated a P-value <0.001, indicating a significant difference. To further identify which specimen type contributes to this significance, we used the residual counts from the Chi-squared test and plotted the outcomes (Figure 4). The results show that non-MDR *A. baumannii* appears more frequently in midstream urine specimens (residual count >2), while it is less commonly found in specimens from tracheal aspirate, sputum, wound, peripheral, and central lines (residual count <-2). In contrast, MDR *A. baumannii* 

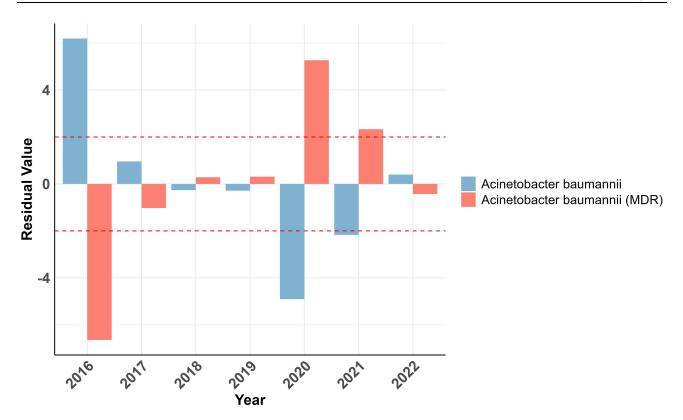
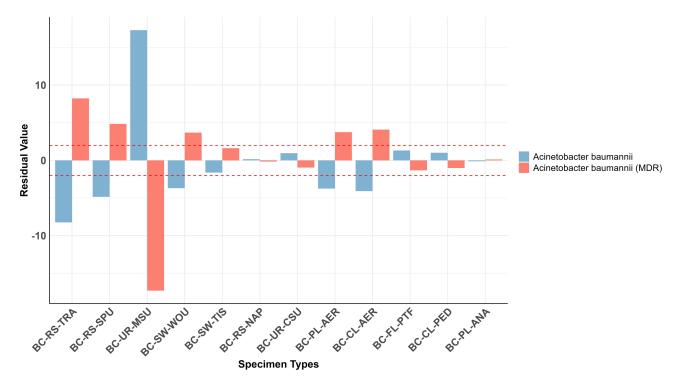


Figure 3 The yearly distribution of cases for non-MDR (blue) and MDR (red) A. baumannii strains from 2016 to 2022. The threshold for the Chi-squared test was set at (-2, 2) for the residual count, with values within this range considered significant, as indicated by the red lines in the figure.



**Figure 4** Distribution of specimen types for non-MDR (blue) and MDR (red) A. *baumannii* strains across the years from 2016 to 2022, highlighting trends and patterns in specimen collection during this period. The threshold for the Chi-squared test was set at (-2, 2) for the residual count, with values within this range considered significant, as indicated by the red lines in the figure.

Abbreviations: BC, Bacterial culture; RS, Respiratory specimen; TRA, Tracheal aspirate; SPU, Sputum; UR, Urine; MSU, Midstream specimen urine; SW, Swab; WOU, Wound; TIS, Tissue; NAP, nasopharyngeal aspirate; CSU, Catheter specimen urine; PL, Peripheral line; AER, Aerobic; FL, Fluids; PTF, Anaerobic; CL, Central line; PDE, Pediatric; ANA, Anaerobic.

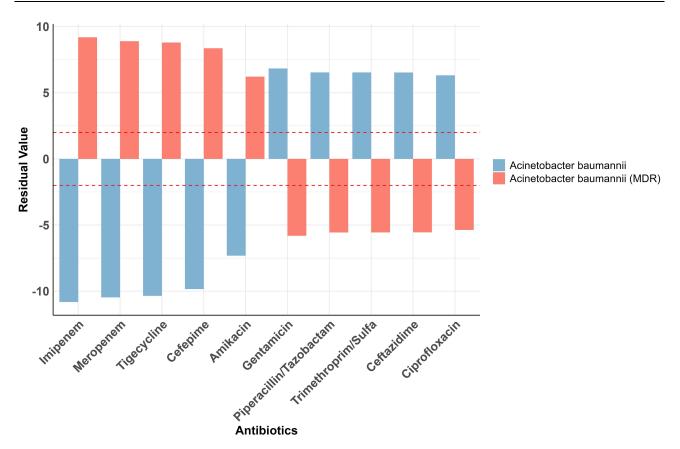


Figure 5 The most antibiotics tested against non-MDR A. baumannii and MDR A. baumannii strains from 2016 to 2022. The threshold for the Chi-squared test was set at (-2, 2) for the residual count, with values within this range considered significant, as indicated by the red lines in the figure.

is more commonly present in tracheal aspirate, sputum, wound, peripheral, and central lines specimens (residual count >2), and less commonly found in midstream urine specimens (residual count <-2).

To evaluate whether there was a significant difference in the effectiveness of antibiotics tested against non-MDR *A. baumannii* and MDR *A. baumannii*, a Chi-squared test was applied (Figure 5). The results indicated a P-value <0.001, indicating a significant difference between antibiotic classes. To determine which antibiotic contributed to this significance, the residual counts from the Chi-squared test were used. The outcomes revealed that the most frequent antibiotics tested with non-MDR *A. baumannii* were, gentamicin, piperacillin/tazobactam, trimethoprim/Sulfamethoxazole, ceftazidime, ciprofloxacin (residual count >2). For MDR *A. baumannii* the most frequent-tested antibiotics were imipenem, meropenem, tigecycline, cefepime, and amikacin (residual count >2). In accordance with the policy established by King Abdulaziz University Hospital, *A. baumannii* strains are labelled as MDR when they exhibit resistance to multiple antibiotic classes, including penicillins, carbapenems, cephalosporins (including inhibitor combinations), fluoroquinolones, and aminoglycosides.<sup>20</sup>

#### Discussion

This six-year retrospective study provides a comprehensive analysis of the epidemiological and clinical patterns associated with *A. baumannii* infections, with an explicit focus on age distribution, antibiotic resistance, and specimen types. By contrasting non-MDR *A. baumannii* infections with their MDR counterparts, this research examines patient data from January 2016 to December 2022 at King Abdulaziz University Hospital, Jeddah.

Our findings indicate a substantial decrease in non-MDR *A. baumannii* infections, suggesting that current infection control protocols and antibiotic stewardship initiatives are effective in limiting infections from less-resistant strains. This trend aligns with global observations, where rigorous infection control and stewardship programs have similarly contributed to reducing nosocomial infections.<sup>21–24</sup> However, the persistence of MDR *A. baumannii* infections over

time highlights a complex interaction between resistance mechanisms and current treatment approaches. This finding corroborates previous studies emphasizing the resilience of MDR strains, which continue to spread despite rigorous infection control efforts.<sup>11,25–28</sup>

Our age analysis revealed distinct patterns in susceptibility to MDR and non-MDR *A. baumannii* infections. The data show a higher incidence of MDR infections among older age groups, particularly in patients aged 70–74, with a notable incidence also in those aged 50–59. This contrasts with non-MDR infections, which were predominantly observed in younger age groups, including paediatric patients. These findings suggest that age-related factors, such as the presence of comorbidities, longer hospital stays, and prior antibiotic exposure, contribute to the heightened vulnerability of older patients to MDR infections. Similar patterns have been documented in the previous research, highlighting the need for age-specific infection prevention strategies to protect at-risk groups.<sup>29–31</sup> These findings underscore the importance of developing targeted strategies to manage infection risks across different age demographics, particularly for elderly patients with chronic conditions.

Our study underscores several key risk factors contributing to the incidence of *A. baumannii* infections in ICU settings, particularly highlighting the roles of intubation, catheterization, immunosuppression, advanced age, extended hospitalization, prior antibiotic exposure, environmental contamination, and the use of invasive medical devices. Intubation, frequently associated with ventilator-associated pneumonia (VAP), is a significant risk factor due to the pathogen's tendency to colonize respiratory equipment. This finding aligns with regional studies, such as Al-Gethamy et al, which reported high rates of *A. baumannii* colonization in intubated patients, illustrating the need for enhanced sterilization protocols in respiratory support devices to reduce VAP risks.<sup>14</sup> Catheter use, particularly central venous catheters (CVCs), also plays a critical role in *A. baumannii* transmission, with our findings showing a strong correlation between catheterization and bloodstream infections. Similar trends were observed, with catheter-related bloodstream infections being identified as a significant issue in ICU environments.<sup>32</sup> This underscores the importance of aseptic protocols for catheter insertion and maintenance in preventing these infections.

Older patients, particularly those with multiple comorbidities, were also found to be at heightened risk, likely due to extended ICU stays and underlying health issues that complicate treatment. Elbehiry et al similarly noted increased *A. baumannii* incidence among older ICU patients, suggesting that age-specific infection control protocols could be beneficial. Extended hospital stays further compound infection risk due to *A. baumannii*'s persistence on environmental surfaces.<sup>11</sup> In line with this, Yasir et al demonstrated that MDR *A. baumannii* can remain viable on ICU surfaces for prolonged periods, emphasizing the need for rigorous and regular cleaning to reduce nosocomial transmission.<sup>27</sup>

Our study highlights substantial resistance to critical antibiotics, including carbapenems, polymyxins, and  $\beta$ -lactams, among *A. baumannii* isolates, presenting a significant challenge in clinical treatment. Carbapenem resistance, largely mediated by  $\beta$ -lactamase enzymes like blaOXA-23 and blaNDM-1, reflects the pathogen's adaptability and poses a major hurdle in ICU treatment. The incidence of blaOXA-23 in carbapenem-resistant isolates has been reported in other studies, such as Shah et al, who noted the presence of this gene alongside insertion elements that increase expression levels. Additionally, polymyxin resistance is emerging, with Raees et al documenting a 24% colistin resistance rate among carbapenem-resistant strains.<sup>26,31</sup> This resistance is often due to mutations in lipid A biosynthesis genes (lpxA, lpxC, and lpxD), which alter the cell membrane and reduce colistin's effectiveness. Further complicating treatment,  $\beta$ -lactam resistance, facilitated by enzymes such as blaADC, reduces the efficacy of third-generation cephalosporins, as shown by Yasir et al.<sup>27</sup> These cumulative resistance mechanisms highlight the urgent need for alternative therapeutic strategies, including combination therapies with novel agents like cefiderocol and the exploration of adjunctive treatments such as antimicrobial peptides and bacteriophage therapy to effectively combat MDR *A. baumannii*.

Our specimen analysis reveals important differences between MDR and non-MDR strains regarding infection sites. MDR *A. baumannii* was predominantly isolated from tracheal aspirates, sputum, wounds, and central lines, indicating a higher tendency for invasive infections. This trend suggests that MDR strains are particularly adept at infecting more invasive sites, posing greater challenges for treatment and patient recovery. Conversely, non-MDR strains were mainly isolated from midstream urine specimens, reflecting a lower degree of invasiveness. These findings align with prior studies suggesting that MDR strains exhibit more versatile infection patterns, allowing them to persist in various hospital environments and anatomical sites.<sup>33,34</sup> These distinctions support targeted infection control strategies based on infection

site. For instance, additional precautions in respiratory and wound care for MDR cases could be beneficial, given the pathogen's frequent presence in tracheal and wound specimens. Furthermore, as MDR strains exhibit higher resistance to last-line antibiotics, our findings suggest the need for more aggressive therapeutic approaches for MDR-infected sites to improve patient outcomes.

The persistence and transmission of *A. baumannii* extend beyond hospital settings, encompassing various environmental, animal, and community reservoirs, highlighting the necessity of a One Health approach. This approach recognizes that human health is interconnected with the health of animals and the environment, suggesting that control efforts must address all potential reservoirs to effectively mitigate the pathogen's spread. Studies such as Yasir et al reveal that carbapenem-resistant *A. baumannii* strains isolated from ICU environments share genetic similarities with strains found in hospital-adjacent areas and on non-medical surfaces, underscoring the pathogen's resilience and adaptability.<sup>27</sup> In addition to environmental persistence, *A. baumannii* is increasingly identified in animal reservoirs, which further supports the need for a One Health approach. Research from Mellace et al highlights the pathogen's ability to colonize livestock and other animals, which may serve as intermediate reservoirs, allowing cross-species transmission and contributing to the reintroduction of MDR strains into healthcare settings.<sup>35</sup>

To combat *A. baumannii* within a One Health framework, integrated strategies across human, animal, and environmental health sectors are essential. Key recommendations include monitoring environmental sources, especially in highrisk areas like ICUs and surrounding healthcare facilities, implementing stricter controls on agricultural antibiotic use, and establishing robust decontamination practices. Additionally, genomic surveillance in animal and environmental samples could help trace the origins and transmission pathways of MDR *A. baumannii*, allowing for more effective interventions across sectors.<sup>36</sup>

While this study provides a robust analysis, certain limitations must be noted. The reliance on retrospective data and the lack of detailed antibiotic sensitivity profiles limits the generalizability of our findings. Additionally, as the study was conducted at a single medical centre, broader epidemiological trends across Saudi Arabia may not be fully represented. Future research should prioritize multicentre studies with genomic analyses to enhance understanding of resistance mechanisms and guide effective treatment protocols. Future directions should also explore the development of novel antimicrobials, alternative therapies, and comprehensive antibiotic stewardship programs across healthcare settings. These programs can help identify best practices to prevent resistance and improve patient care. Continued genomic surveillance will provide insights into resistance evolution and enable more targeted intervention strategies.

In conclusion, our study highlights the critical need for ongoing surveillance and adaptable infection control strategies to address the persistent challenge of MDR *A. baumannii*. The data reveal age-related susceptibility differences, with older patients facing higher infection risks, underscoring the importance of targeted preventive measures. The pronounced resistance to carbapenems and polymyxins in MDR strains stresses the urgency of exploring alternative treatments and combination therapies. Our findings also support the One Health approach, which considers environmental, animal, and human reservoirs, to contain *A. baumannii* more comprehensively. Future efforts should focus on integrated antibiotic stewardship and genomic surveillance across healthcare settings to inform policy and improve patient outcomes.

#### Disclosure

The authors report no conflicts of interest in this work.

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