Infection and Drug Resistance

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ORIGINAL RESEARCH

Risk Factors, Outcomes, and Predictions of Extensively Drug-Resistant *Acinetobacter baumannii* Nosocomial Infections in Patients with Nervous System Diseases

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Purpose: *Acinetobacter baumannii* has evolved to become a major pathogen of nosocomial infections, resulting in increased morbidity and mortality. This study aimed to investigate the risk factors, outcomes, and predictions of extensively drug-resistant (XDR)-*A. baumannii* nosocomial infections in patients with nervous system diseases (NSDs).

Methods: A retrospective study of patients infected with XDR-*A. baumannii* admitted to the Affiliated Hospital of Southwest Medical University (Luzhou, China) from January 2021 to December 2022 was conducted. Three multivariate regression models were used to assess the risk factors and predictive value for specific diagnostic and prognostic subgroups.

Results: A total of 190 patients were included, of which 84 were diagnosed with NSDs and 80% of those were due to stroke. The overall rates of all-cause mortality for XDR-*A. baumannii* nosocomial infections and those in NSDs were 38.9% and 40.5%, respectively. Firstly, hypertension, indwelling gastric tube, tracheotomy, deep puncture, bladder irrigation, and pulmonary infections were independent risk factors for XDR-*A. baumannii* nosocomial infections in patients with NSDs. Moreover, pulmonary infections, the aspartate aminotransferase (AST) to alanine aminotransferase (ALT) ratio, and the neutrophil-to-lymphocyte ratio (NLR) were significantly associated with increased mortality rates in patients with nosocomial infections caused by XDR-*A. baumannii*. Thirdly, NLR and cardiovascular diseases accounted for a high risk of mortality for XDR-*A. baumannii* nosocomial infections in patients with NSDs. The area under the curves of results from each multivariate regression model were 0.827, 0.811, and 0.853, respectively.

Conclusion: This study reveals the risk factors of XDR-*A. baumannii* nosocomial infections in patients with NSDs, and proves their reliable predictive value. Early recognition of patients at high risk, sterilizing medical tools, and regular blood monitoring are all critical aspects for minimizing the nosocomial spread and mortality of *A. baumannii* infections.

Keywords: risk factors, mortality, prediction, extensively drug-resistant *Acinetobacter baumannii*, nosocomial infection, nervous system diseases

Introduction

Acinetobacter baumannii is an opportunistic pathogen responsible for a wide range of nosocomial infections. *A. baumannii* has the ability to adapt to the environment and resist various cleaning and disinfecting methods, and therefore is widely distributed and able to survive for prolonged periods in hospitals.[1,2] *A. baumannii* is one of the most important hospital pathogens, usually found mainly in the intensive care unit (ICU), affecting debilitated patients with weakened immune systems and/or imbalances of the normal flora, with pneumonia and bacteremia being the most common clinical manifestations.[3,4] Indeed, *A. baumannii*, which has an exceptional ability to acquire multi-, extensive-,

Received: 29 September 2023
Accepted: 11 November 2023
Published: 22 November 2023

and pan-drug resistance phenotypes through the acquisition of mobile genetic elements, is one of the most drug-resistant organisms that are currently encountered in clinical practice.[4,5] It has been observed that the global prevalence of *A. baumannii* infections is growing annually, and more than half of them are carbapenem-resistant, which greatly reduces the selectivity of antibiotics and the chances of a successful treatment.[6,7]

The human nervous system is distributed throughout the body, including the central nervous system (CNS) and the peripheral nervous system (PNS). The CNS is composed of the brain and the spinal cord, which process the information they receive and generate, and then transmit it to the periphery through motor outputs. The PNS consists of neurons and their cellular processes that are responsible for relaying sensory data from the periphery to the CNS. Moreover, there are autonomic pathways of efferent and afferent between these two compartments. By supplying innervation to the muscle through the spinal cord motor neurons and the neuromuscular junction, voluntary motor activities are enabled in the periphery.[8] Nervous system diseases (NSDs) are the primary cause of disability and the second most frequent cause of death worldwide, especially in low- and middle-income countries. In addition, the growing social and economic burdens of NSDs are attributed to global population growth and aging.[9,10] Patients with NSDs usually have a long duration and a severe illness, and mostly lack effective treatments.[11] If a patient develops nosocomial bacterial infections during a prolonged hospital stay, it will certainly lead to a poorer prognosis and increased mortality.[12]

To date, there are few studies focusing on extensively drug-resistant (XDR)-*A. baumannii* nosocomial infections in patients with NSDs. Therefore, the aim of this study was to summarize the clinical characteristics and outcomes of patients infected with XDR-*A. baumannii* during hospitalization, and explore the risk factors and prognosis of XDR-*A. baumannii* nosocomial infections in patients with NSDs, as well as evaluate the predictive values of the results.

Materials and Methods

Study Design and Population Selection

A retrospective study including patients with *A. baumannii* infections between January 2021 and December 2022 admitted to the Affiliated Hospital of Southwest Medical University (Luzhou, China), which is a 4200-bed tertiary hospital with 65 wards and approximately 134,000 annual admissions.[13] Patients with XDR-*A. baumannii* nosocomial infections were categorized into a NSD group and a non-NSD group based on their admission diagnosis. Inclusion criteria for all patients were: (1) positive culture of XDR-*A. baumannii* from samples obtained from patients after 48 hours of admission; (2) clinical signs and symptoms consistent with infection; (3) clearly diagnosis of NSDs; (4) complete medical record information. In addition, patients who met the above criteria were categorized into a death group (all-cause mortality during hospitalization) and a survival group (cure or improvement during hospitalization) based on their clinical outcome. Meanwhile, patients with XDR-*A. baumannii* among the NSD group were further categorized into the death and survival groups according to the same requirements.

Identification and Antimicrobial Susceptibility Testing

All clinical samples obtained from selected patients were sent to the microbiology laboratory in a timely manner after collection, with inoculation and culturing of the samples completed within two hours, and all procedures were performed using aseptic technique. All *A. baumannii* were identified by matrix-assisted laser desorption/ionization time-of-flight spectrometry (Bruker, Germany), and antimicrobial susceptibility testing for conventional antibiotics was performed using the MicroScan Walk-Away 96 Plus system (Beckman Coulter, USA). Twenty-one antimicrobial agents, including amikacin, cefepime, imipenem, piperacillin/tazobactam, ceftriaxone, ampicillin/sulbactam, cefotaxime, ciprofloxacin, gentamicin, piperacillin, ticarcillin/clavulanic acid, tobramycin, ceftazidime, meropenem, levofloxacin, ampicillin, tetracycline, trimethoprim-sulfamethoxazole, tigecycline, cefoperazone/sulbactam, and polymyxin B, were tested for all *A. baumannii* strains. The results were interpreted according to the Clinical and Laboratory Standards Institute (CLSI) M100. XDR was defined as non-susceptibility to ≥ 1 agent but ≤ 2 antimicrobial categories.[14]

Data Collection

All data were collected from the hospital computerized database. The following information was reviewed: demographics, underlying diseases, invasive procedures, comorbid conditions, clinical and antibiotic therapies, laboratory findings, microbiological data, hospital costs, and clinical outcomes. In detail, demographics include sex, age, length of hospital stay, previous 6-month history of hospitalization, cigarette smoking, and alcohol consumption. Underlying diseases contain diabetes, hypertension, liver diseases, kidney diseases, tumors, hematologic diseases, and pancreatitis. Indwelling gastric tube, indwelling urinary catheter, mechanical ventilation, central venous catheter, tracheotomy, deep puncture, catheter drainage, fiberoptic bronchoscope, and bladder irrigation were included in invasive procedures. Laboratory findings include albumin, albumin to globulin ratio, aspartate aminotransferase (AST) to alanine aminotransferase (ALT) ratio (AST/ALT ratio), leukocyte count, neutrophil percentage, lymphocyte percentage, neutrophil-to-lymphocyte ratio (NLR), C-reactive protein, serum amyloid A (SAA), and procalcitonin (PCT). All results were tested on the same day as the positive XDR-*A. baumannii* culture collection. Microbiological data include the sample type and drug-resistance profile. Clinical outcomes include cure (complete resolution of symptoms and no need for further antimicrobial therapy), improvement (partial resolution of symptoms and signs), and failure (prolonged or worsening of symptoms and signs, or death).

Statistical Analysis

All data were analyzed using the Statistical Product and Service Solutions (SPSS) version 23. Categorical variables were expressed as frequencies and percentages, and continuous variables were expressed as mean±standard deviation (SD) or median and interquartile range (IQR). In univariate analysis of variance, categorical variables were analyzed using Chi-square tests or Fisher's exact tests, and continuous variables using t-tests or the Wilcoxon rank-sum tests. $P < 0.05$ was considered to be statistically significant and was included in multivariate models. Independent risk factors among subgroups were analyzed using multivariate logistic regression, and statistically significant factors were further used to establish the risk prediction models. The goodness-of-fit of models was checked using the Hosmer-Lemeshow test. The resulting β-coefficients of the significant predictors were then used to assign values; the coefficient with the lowest value was given a score of 1, and the others were given rounded scores.[15] The receiver operating characteristic (ROC) curve was used to assess the model and calculate the cutoff values, and the corresponding area under the curve (AUC) was used to test the overall predictive ability. In general, a factor with $0.7 < AUC < 0.9$ indicates a moderate discriminatory value.[16] The final results were presented using the *P*-values, odds ratio (OR), and 95% confidence intervals (CI).

Results

Microbiological Information and Patient Characteristics

Out of the 850 *A. baumannii* strains isolated from the patients after hospitalization during the study period, 190 strains were identified as XDR and met all the inclusion criteria. Among these XDR-*A. baumannii* strains, 144 strains (75.8%) were isolated from sputum, followed by secretions (9.5%), blood (4.2%), bronchoalveolar lavage fluid (3.2%), urine (1.6%), thoracic/abdominal effusions (1.6%), peripherally inserted central venous catheters (1.6%), and other sources (2.5%). Furthermore, among enrolled patients, 143 were males and 47 were females, with a median age of 62.50 years. The mean length of hospital stay was 30.00 days. 32.63% of patients (n = 62) had a history of cigarette smoking, 21.05% of patients (n = 40) had a history of alcohol consumption, and 20.53% of patients (n = 39) had been hospitalized in the previous 6 months. The most common underlying disease was hypertension (n = 92, 48.42%), followed by diabetes (n = 39, 20.53%) and tumors (n = 25, 13.16%). Regarding the type of invasive procedures, most patients received indwelling urinary catheter (n = 174, 91.58%) and 161 patients (84.74%) underwent indwelling gastric tube. 96.84% of patients (n = 184) received a combination of antibiotic therapies. The most frequent comorbid condition was pulmonary infection (n = 161, 84.74%) and 143 (75.26%) patients had co-infection with other microorganisms. The median hospital cost was 120908.50 CYN.

Based on admission etiology and treatment outcomes, 84 (44.2%) patients were classified as the NSD group and 106 as the non-NSD group (55.8%). The most common neurological condition in the NSD group was stroke (both ischemic

and hemorrhagic), accounting for 80% of cases. Moreover, 74 patients (38.9%) were confirmed dead, while 116 (61.1%) survived. Among the 84 patients of XDR-*A. baumannii* nosocomial infections in the NSD group, 34 (40.5%) ended in death, and 50 (59.5%) survived.

Risk Factors and Predictions for XDR-*A. Baumannii* Nosocomial Infections in Patients with NSDs

Table 1 summarizes the clinical characteristics as well as the results of univariate and multivariate analysis between the NSD and non-NSD groups. In the univariate analysis, the results showed that patients in the NSD group had a longer hospital stay ($P < 0.001$) and had a higher probability of having hypertension as an underlying condition ($P = 0.032$). Patients had received more invasive procedures, including indwelling gastric tube ($P = 0.006$), tracheotomy ($P < 0.001$), deep puncture ($P < 0.001$), catheter drainage ($P = 0.005$), bladder irrigation ($P = 0.022$), and aspiration of sputum therapy ($P = 0.019$) during hospitalization. Moreover, pulmonary infections ($P < 0.001$) were also observed more frequently in patients with NSDs. Conversely, patients in the non-NSD group had more prior 6-month hospitalization histories ($P < 0.001$) and more underlying conditions, such as tumors ($P = 0.009$) and pancreatitis ($P = 0.025$), than those in the NSD group. During hospitalization, patients without NSDs received more invasive procedures with fiberoptic bronchoscope ($P < 0.001$) as well as blood transfusions ($P = 0.019$) and hormone therapy ($P = 0.013$), and more patients developed comorbidities of respiratory failure ($P = 0.004$), cardiovascular diseases ($P = 0.018$), sepsis ($P < 0.001$), abdominal infections ($P = 0.001$), and septic shock ($P < 0.001$). The patients with NSDs had a lower level of leukocyte count ($P = 0.021$), neutrophil percentage ($P = 0.006$), NLR ($P = 0.014$), and PCT ($P = 0.011$), whereas a higher level of lymphocyte percentage ($P = 0.015$). Multivariate logistic regression revealed that hypertension (OR = 6.013, 95% CI: 1.178–30.699, $P = 0.031$), indwelling gastric tube (OR = 25.019, 95% CI: 1.626–384.926, $P = 0.021$), tracheotomy (OR = 10.161, 95% CI: 2.080–49.652, $P = 0.004$), deep puncture (OR = 10.340, 95% CI: 1.072–99.781, $P = 0.043$), bladder irrigation (OR = 14.517, 95% CI: 1.417–148.684, $P = 0.024$), and pulmonary infections (OR = 218.510, 95% CI: 11.429–4177.591, $P < 0.001$) were independent risk factors associated with XDR-*A. baumannii* nosocomial infections in patients with NSDs.

The goodness of fit of the multivariate model was 0.980. The AUC was 0.827 (95% CI: 0.769–0.884), indicating an adequate prediction ability of XDR-*A. baumannii* nosocomial infections in patients with NSDs. The sensitivity and specificity of this prediction model were 0.631 and 0.849, respectively (Figure 1A).

Risk Factors and Prediction of Mortality in Patients with XDR-*A. Baumannii* Nosocomial Infections

The results of univariate and multivariate analysis for different outcomes among patients with XDR-*A. baumannii* nosocomial infections are listed in Table 2. The overall all-cause mortality in patients with XDR-*A. baumannii* nosocomial infections was 38.9%. Patients in the death group were older (69.00 vs 57.00) ($P < 0.001$) than those in the survival group. The deceased had a higher incidence of diabetes ($P = 0.032$), underwent more invasive procedures during hospitalization (indwelling gastric tube [$P = 0.009$], deep puncture [$P = 0.049$], and fiberoptic bronchoscope [$P = 0.030$]), and presented more comorbidities (respiratory failure [$P < 0.001$], cardiovascular diseases [$P < 0.001$], sepsis [$P = 0.002$], pulmonary infections [$P = 0.001$], and septic shock [$P = 0.001$]) than those who survived. All deceased patients experienced aspiration of sputum therapy ($P = 0.002$). Regarding the results of blood testing, the AST/ALT ratio ($P = 0.028$), leukocyte count ($P = 0.003$), NLR ($P < 0.001$), and PCT ($P = 0.003$) were significantly higher in deceased patients. Multivariate analysis evaluated the in-hospital mortality in patients with XDR-*A. baumannii* nosocomial infections was significantly associated with pulmonary infections (OR = 4.690, 95% CI: 1.039-21.181, $P = 0.045$), the AST/ALT ratio (OR = 1.718, 95% CI: 1.076–2.741, $P = 0.023$), and NLR (OR = 1.058, 95% CI: 1.013–1.104, $P = 0.011$).

The goodness of fit of the multivariate model was 0.180. The AUC was 0.811 (95% CI: 0.749–0.872), suggesting an adequate prediction ability of mortality in patients with XDR-*A. baumannii* nosocomial infections. The sensitivity was 0.865 and specificity was 0.672 for this prediction model (Figure 1B).

Table 1 Clinical Characteristics and Univariate/Multivariate Analysis of XDR-*A. Baumannii* Nosocomial Infections in Patients with NSDs

Variables	All Patients (n=190)	NSDs (n=84)	Non-NSDs (n=106)	Univariate Analysis	Multivariate Analysis	
				P-value	OR (95% CI)	*P*-value
Demographics						
Sex, n (%)						
Male, n (%)	143 (75.26%)	66 (78.57%)	77 (72.64%)	0.347		
Female, n (%)	47 (24.74%)	18 (21.43%)	29 (27.36%)			
Age (year), median (IQR)	62.50 (51.00–73.75)	58.00 (47.00–72.50)	65.00 (52.50–75.00)	0.830		
Length of hospital stay (day), median (IQR)	30.00 (16.00–46.50)	34.50 (24.00–57.50)	25.50 (13.25–37.00)	<0.001	1.017 (0.993–1.041)	0.162
Previous 6-month history of hospitalization	39 (20.53%)	4 (4.76%)	35 (33.02%)	<0.001	0.018 (0.001–0.257)	0.003
Cigarette smoking, n (%)	62 (32.63%)	26 (30.95%)	36 (33.96%)	0.660		
Alcohol consumption, n (%)	40 (21.05%)	14 (16.67%)	26 (24.53%)	0.187		
Underlying diseases						
Diabetes mellitus, n (%)	39 (20.53%)	15 (17.86%)	24 (22.64%)	0.417		
Hypertension, n (%)	92 (48.42%)	48 (57.14%)	44 (41.51%)	0.032	6.013 (1.178–30.699)	0.031
Liver Diseases, n (%)	16 (8.42%)	6 (7.14%)	10 (9.43%)	0.572		
Kidney Diseases, n (%)	13 (6.84%)	5 (5.92%)	8 (7.55%)	0.665		
Tumors, n (%)	25 (13.16%)	5 (5.95%)	20 (18.87%)	0.009	0.024 (0.001–0.387)	0.009
Hematologic diseases, n (%)	1 (0.53%)	0 (0.00%)	1 (0.94%)	0.372		
Pancreatitis, n (%)	10 (5.26%)	1 (1.19%)	9 (8.50%)	0.025	0.344 (0.007–16.002)	0.586
Invasive procedures						
Indwelling gastric tube, n (%)	161 (84.74%)	78 (92.86%)	83 (78.30%)	0.006	25.019 (1.626–384.926)	0.021
Indwelling urinary catheter, n (%)	174 (91.58%)	78 (92.86%)	96 (90.57%)	0.572		
Mechanical ventilation, n (%)	159 (83.68%)	67 (79.76%)	92 (86.79%)	0.193		
Central venous catheter, n (%)	154 (81.05%)	70 (83.33%)	84 (79.25)	0.475		
Tracheotomy, n (%)	75 (39.47%)	53 (63.10%)	22 (20.75%)	<0.001	10.161 (2.080–49.652)	0.004
Deep puncture, n (%)	91 (47.89%)	55 (61.90%)	36 (33.96%)	<0.001	10.340 (1.072–99.781)	0.043
Catheter drainage, n (%)	74 (38.95%)	42 (50.00%)	32 (30.19%)	0.005	0.427 (0.039–4.640)	0.485
Fiberoptic bronchoscope, n (%)	62 (32.63%)	16 (19.05%)	46 (43.40%)	<0.001	0.165 (0.037–0.739)	0.019
Bladder irrigation, n (%)	30 (15.79%)	19 (22.62%)	11 (10.38%)	0.022	14.517 (1.417–148.684)	0.024
Comorbid conditions						
Respiratory failure, n (%)	90 (47.37%)	30 (35.71%)	60 (56.60%)	0.004	0.252 (0.054–1.166)	0.078
Hypoproteinemia, n (%)	138 (72.63%)	65 (77.38%)	73 (68.87%)	0.191		
Cardiovascular diseases, n (%)	55 (28.95%)	17 (20.24%)	38 (35.85%)	0.018	0.433 (0.092–2.035)	0.289
Anemia, n (%)	120 (63.16%)	54 (64.29%)	66 (62.26%)	0.774		
Sepsis, n (%)	46 (24.21%)	4 (4.76%)	42 (39.62%)	<0.001	0.020 (0.002–0.235)	0.002
Mixed infections, n (%)	143 (75.26%)	64 (76.19%)	79 (74.83%)	0.792		
Bacteremia, n (%)	4 (2.11%)	2 (2.38%)	2 (1.89%)	0.814		

(*Continued*)

https://doi.org/10.2147/IDR.S439241

Table 1 (Continued).

Variables	All Patients (n=190)	NSDs (n=84)	Non-NSDs (n=106)	Univariate Analysis	Multivariate Analysis	
				P-value	OR (95% CI)	*P*-value
Pulmonary infections, n (%)	161 (84.74%)	81 (96.43%)	80 (75.47%)	<0.001	218.510 (11.429–4177.591)	<0.001
Abdominal infections, n (%)	12 (6.32%)	0 (0.00%)	12 (11.32%)	0.001	-	0.998
Septic shock, n (%)	26 (13.68%)	1 (1.19%)	25 (23.58%)	<0.001	0.642 (0.015–26.760)	0.816
Clinical and antibiotic therapies						
Hormone, n (%)	116 (61.05%)	43 (51.19%)	73 (68.87%)	0.013	0.521 (0.102–2.650)	0.432
Proton pump inhibitor, n (%)	138 (72.63%)	65 (77.38%)	73 (68.87%)	0.191		
Aspiration of sputum, n (%)	176 (92.63%)	82 (97.62%)	94 (88.68%)	0.019	2.416 (0.089–65.380)	0.600
Combination of antibiotics, n (%)	184 (96.84%)	81 (96.43%)	103 (97.17%)	0.772		
Blood transfusion, n (%)	95 (50.00%)	34 (40.48%)	61 (57.55%)	0.019	0.807 (0.203–3.210)	0.761
Erythrocytes, n (%)	80 (42.11%)	30 (88.24%)	50 (81.97%)			
Plasma, n (%)	60 (31.58%)	17 (50.00%)	43 (70.49%)			
Platelets, n (%)	6 (3.16%)	2 (5.88%)	4 (6.56%)			
Other information						
Be critically ill, n (%)	175 (92.11%)	78 (92.86%)	97 (91.51%)	0.732		
ICU admission, n (%)	129 (67.89%)	58 (69.05%)	71 (66.98%)	0.762		
Laboratory findings						
Albumin (g/L), mean±SD	32.48±0.41	37.18±32.53	31.41±5.25	0.074		
A/G, mean±SD	1.31±0.03	1.29±0.30	1.31±0.38	0.661		
AST/ALT, median (IQR)	1.10 (0.78–1.73)	1.1 (0.75–1.79)	1.09 (0.78–1.72)	0.660		
Leukocyte count (10^9/L), median (IQR)	11.87 (7.90–15.48)	11.22 (7.46–14.33)	12.44 (8.14–16.79)	0.021	0.964 (0.849–1.094)	0.569
Neutrophil (%), median (IQR)	85.10 (77.10–89.45)	82.60 (75.90–88.25)	86.60 (78.73–90.48)	0.006	0.811 (0.655–1.005)	0.056
Lymphocyte (%), median (IQR)	7.85 (5.13–13.05)	9.65 (6.00–14.78)	7.40 (4.63–11.98)	0.015	0.865 (0.661–1.133)	0.292
NLR, median (IQR)	10.59 (5.85–17.73)	8.67 (5.19–14.66)	11.67 (6.75–19.95)	0.014	1.078 (0.970–1.197)	0.165
C-reactive protein (mg/L), median (IQR)	50.36 (17.55–102.16)	40.10 (12.95–102.07)	57.96 (21.11–102.16)	0.225		
Serum amyloid A (mg/L), median (IQR)	232.78 (69.24–308.96)	248.70 (58.98–300.00)	231.64 (72.57–431.09)	0.236		
Procalcitonin (ng/mL), median (IQR)	0.63 (0.21–2.17)	0.42 (0.21–1.05)	1.00 (0.22–3.64)	0.011	1.007 (0.909–1.116)	0.893
Hospital costs (thousand CNY), median (IQR)	120.91 (60.40–199.60)	139.88 (92.79–201.85)	92.77 (47.69–199.60)	0.050		

Abbreviations: OR, odds ratio; CI, confidence interval; IQR, interquartile range; ICU, intensive care unit; A/G, albumin to globulin ratio; AST/ALT ratio, aspartate aminotransferase to alanine aminotransferase ratio; NLR, neutrophil-to-lymphocyte ratio.

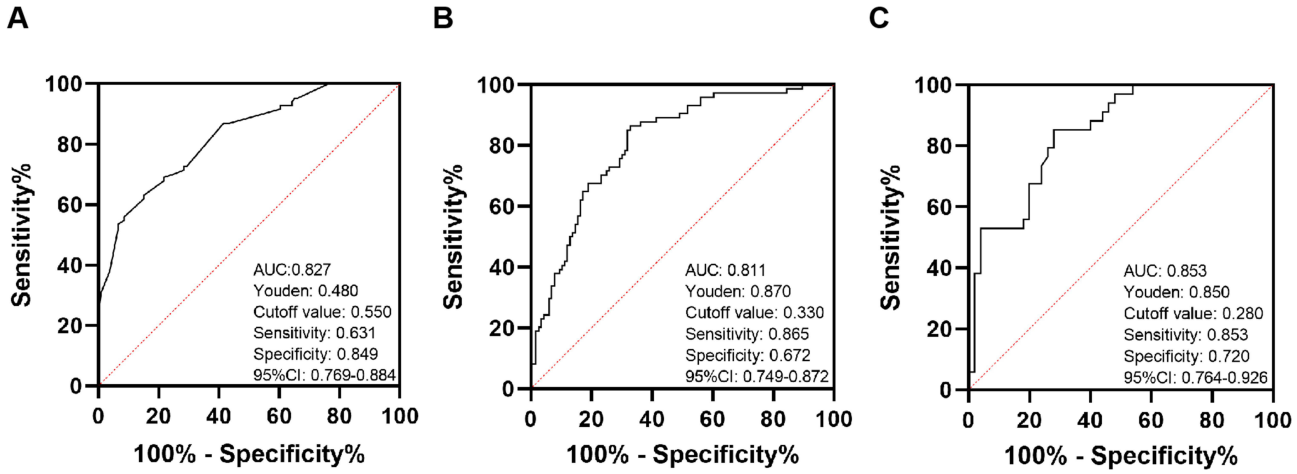

Figure 1 The receiver operating characteristic curves for predicting XDR-*A. baumannii* nosocomial infections in different groups. (**A**) patients with NSDs; (**B**) patients with all-cause mortality; (**C**) mortality among patients with NSDs.
Abbreviations: AUC, area under the curve; CI, confidence interval.

Risk Factors and Prediction of Mortality in Patients with XDR-*A. Baumannii* Nosocomial Infections Among the NSD Group

The overall all-cause mortality in patients with XDR-*A. baumannii* nosocomial infections among the NSD group was 40.5%. As shown in Table 3, mortality was more prone in patients who were older ($P = 0.014$). Respiratory failure ($P = 0.024$) and cardiovascular diseases ($P = 0.001$) were 2 times and 4.8 times more common, respectively, in the death group than in the survivor group. In addition, an increase in the AST/ALT ratio ($P = 0.035$), NLR ($P < 0.001$), and SAA ($P = 0.004$) were observed in patients in the death group. According to multivariate analysis, NLR (OR = 1.150, 95% CI: 1.032–1.282, $P = 0.011$) and cardiovascular diseases (OR = 7.948, 95% CI: 1.112–56.832, $P = 0.039$) were significantly correlated with mortality in patients with XDR-*A. baumannii* nosocomial infections among the NSD group.

The goodness of fit of the multivariate model was 0.408. Moreover, this model could adequately predict the mortality in patients with XDR-*A. baumannii* nosocomial infections among the NSD group (AUC=0.853, 95% CI: 0.764–0.926), and the sensitivity and specificity were 85.3% and 72.0%, respectively (Figure 1C).

Table 2 Risk Factors of Mortality in Patients with XDR-*A. Baumannii* Nosocomial Infections

Variables	Non-Survivor (n=74)	Survivor (n=116)	Univariate Analysis	Multivariate Analysis	
			P-value	OR (95% CI)	*P*-value
Age (year), median (IQR)	69.00 (57.00–77.00)	57.00 (48.00–69.50)	<0.001	1.028 (0.998–1.059)	0.064
Diabetes mellitus, n (%)	21 (28.38%)	18 (15.52%)	0.032	1.226 (0.461–3.259)	0.682
Indwelling gastric tube, n (%)	69 (93.24%)	92 (79.31%)	0.009	0.771 (0.163–3.635)	0.742
Deep puncture, n (%)	37 (50.00%)	54 (46.55%)	0.049	1.220 (0.534–2.784)	0.637
Fiberoptic bronchoscope, n (%)	31 (41.89%)	31 (26.72%)	0.030	0.882 (0.378–2.058)	0.771
Respiratory failure, n (%)	49 (66.22%)	41 (35.34%)	<0.001	1.092 (0.454–2.626)	0.845
Cardiovascular diseases, n (%)	34 (45.95%)	21 (18.10%)	<0.001	2.064 (0.763–5.585)	0.154
Sepsis, n (%)	27 (36.49%)	19 (16.38%)	0.002	2.015 (0.710–5.718)	0.188
Pulmonary infections, n (%)	**71 (95.95%)**	**90 (77.59%)**	**0.001**	**4.690 (1.039–21.181)**	**0.045**
Septic shock, n (%)	18 (24.32%)	8 (6.90%)	0.001	1.979 (0.502–7.806)	0.330
Aspiration of sputum, n (%)	74 (100.00%)	102 (87.93%)	0.002	-	0.998
AST/ALT, median (IQR)	**1.24 (0.79–2.13)**	**1.07 (0.75–1.61)**	**0.028**	**1.718 (1.076–2.741)**	**0.023**
Leukocyte count (10^9/L), median (IQR)	13.35 (9.37–16.84)	10.22 (6.79–15.19)	0.003	1.047 (0.974–1.125)	0.214
NLR, median (IQR)	**14.88 (10.52–22.05)**	**7.21 (4.52–13.82)**	**<0.001**	**1.058 (1.013–1.104)**	**0.011**
Procalcitonin (ng/mL), median (IQR)	1.10 (0.22–4.49)	0.42 (0.21–1.52)	0.003	1.036 (0.980–1.095)	0.211

Note: Bold indicates statistically significant.
Abbreviations: OR, odds ratio; CI, confidence interval; IQR, interquartile range; AST/ALT ratio, aspartate aminotransferase to alanine aminotransferase ratio; NLR, neutrophil-to-lymphocyte ratio.

Table 3 Risk Factors of Mortality in Patients with XDR-A. Baumannii Nosocomial Infections Among the NSD Group

Variables	Non-Survivor (n=34)	Survivor (n=50)	Univariate Analysis	Multivariate Analysis	
			P-value	OR (95% CI)	*P*-value
Age (year), median (IQR)	68.00 (57.00–74.00)	54.00 (45.00–70.00)	0.014	1.000 (0.959–1.043)	0.996
Respiratory failure, n (%)	17 (50.00%)	13 (26.00%)	0.024	1.201 (0.300–4.815)	0.796
Cardiovascular diseases, n (%)	**13 (38.24%)**	**4 (8.00%)**	**0.001**	**7.948 (1.112–56.832)**	**0.039**
AST/ALT, median (IQR)	1.16 (0.83–2.33)	1.09 (0.68–1.65)	0.035	1.274 (0.642–2.528)	0.488
NLR, median (IQR)	**14.08 (9.70–23.52)**	**5.83 (3.78–9.06)**	**<0.001**	**1.150 (1.032–1.282)**	**0.011**
Serum amyloid A (mg/L), median (IQR)	300.00 (0.21–1.39)	144.15 (0.21–1.05)	0.004	1.003 (0.997–1.008)	0.325

Note: Bold indicates statistically significant.
Abbreviations: OR, odds ratio; CI, confidence interval; IQR, interquartile range; AST/ALT ratio, aspartate aminotransferase to alanine aminotransferase ratio; NLR, neutrophil-to-lymphocyte ratio.

Discussion

The development of multiple antibiotic resistance mechanisms in *A. baumannii* is a major concern in the healthcare system. The World Health Organization has classified carbapenem-resistant *A. baumannii* as a major focus for the development of new antibiotics.[17] In the current study, samples from 850 patients admitted to the Southwest Medical University Hospital between January 2021 and December 2022 revealed the presence of *A. baumannii*, with 22% of them being XDR. Such a high prevalence of XDR is worldwide, with around 25% in the Amazon Region and Chile,[18,19] reaching 55–67% in the rest of China,[20,21] 80% in Bolivia,[22] and even 91% in Iran.[23] *A. baumannii* is commonly thought to cause serious nosocomial infections in immuno-compromised and critically ill patients, such as those in the ICU. Notably, this study found that 44.2% of clinically isolated XDR-*A. baumannii* were from patients with NSDs, a group whose susceptibility had previously gone unappreciated. NSDs are intricate disorders affecting the nervous system, although the precise molecular mechanisms behind them are still not clear.[24] Stroke is the most frequent type of NSDs and is the leading cause of death and disability. Additionally, four-fifths of NSDs patients in this research were suffering from stroke. It has been discovered that stroke initiates a neuroinflammatory process in the brain, which is responsible for the excessive activation of the autonomic nervous system and the subsequent systemic immunodepression. Immunodepression is characterized by lymphopenia as well as malfunctioning of the innate and adaptive immune cells, leading to weakened antibacterial defenses that render patients with stroke susceptible to infections.[25]

In this study, hypertension, pulmonary infections, indwelling gastric tube, tracheotomy, bladder irrigation, and deep puncture were found to be independent risk factors for XDR-*A. baumannii* nosocomial infection in patients with NSDs. Hypertension is frequent in the stroke population and the most crucial modifiable risk factor for strokes. Hypertension promotes stroke by increasing shear stress, damaging endothelial function, and hardening the large arteries. Moreover, hypertension can also contribute to cerebral small vessel disease in various mechanisms, including hypoperfusion, reduced autoregulatory capacity, and increased permeability of the blood-brain barrier.[26] The presence of hypertension aggravates the condition of patients with NSDs, which may increase the probability of bacterial infection during hospitalization. Therefore, patients with NSDs who have hypertension should have their blood pressure monitored regularly during hospitalization and remain on antihypertensive therapy to reduce the risk of infections. Pneumonia is one of the most common infections following strokes, affecting 14% of patients and associated with increased in-hospital mortality, length of stay, and healthcare costs.[27] Giuliano et al's study found that the incidence of pneumonia is much greater among stroke patients than in the general hospital population.[28] Furthermore, a systematic review of the microbiological causes of stroke-associated pneumonia involving 15 studies revealed that the frequency of positivity of cultures in patients with pneumonia was quite varied (15%-88%), with *A. baumannii* being one of the most commonly detected pathogens.[29] In addition, invasive procedures have been determined to predispose both infections among stroke patients and *A. baumannii* nosocomial infections, which is consistent with the results of this study.[25,30] Our study categorized invasive procedures in detail and figured out that indwelling gastric tube, tracheotomy, bladder irrigation, and deep puncture were all significantly associated with XDR-*A. baumannii* infections in patients with NSDs. A variety of invasive procedures are used for the treatment and even life support of patients with NSDs, and *A. baumannii* is one of the most prevalent sources of contamination of medical equipment and tools in hospitals, such as on respiratory care

equipment and laryngoscope blades.[31] Similarly, studies by Ardoino et al[32] and Gethamy et al[33] also illustrated that invasive procedures were significantly associated with nosocomial infections and the transmission of drug-resistant *A. baumannii*. Greater attention should be given to the professional training of healthcare workers, the control of environmental hygiene, and the sterilization of medical devices, which are critical for both intervention and treatment of nosocomial infections relevant to invasive procedures.

Next, the AST/ALT ratio, NLR, and pulmonary infections have proved to be independent risk factors for mortality of XDR-*A. baumannii* nosocomial infections. It is widely known that AST and ALT are the major circulating enzymes in the serum. The AST/ALT ratio is a marker of liver cell damage and death, as well as being associated with other non-liver diseases such as cancers, diabetes, peripheral vascular diseases, acute stroke, and infectious diseases.[34] A previous study has revealed that the AST/ALT ratio was consistently higher among patients with septic shock and was a reliable tool for diagnosing septic shock. Furthermore, the AST/ALT ratio >1.8 was associated with an increased risk of 30-d all-cause mortality of sepsis or septic shock.[35] In this study, sepsis and septic shock were significantly more prevalent among those who passed away compared to those who survived, and the AST/ALT ratio was 1.24 in the non-survival group in contrast to only 1.07 in the survival group. Another retrospective study that included 183 patients also found that the AST/ALT ratio was associated with increased mid-term mortality at 180 d in septic patients.[36] In addition, many studies have confirmed that the NLR usually increases with disease progression and is gaining more attention as a low-cost biomarker of inflammation and prognosis, as well as being more reliable in predicting survival than either the neutrophil count or the lymphocyte count alone.[37,38] This study showed that non-survivors in XDR-*A. baumannii* nosocomial infections had a significantly higher NLR than survivors, which was consistent with other studies about infectious diseases such as bacteremia and spinal epidural abscesses.[39] Since AST/ALT ratio and NLR can be obtained quickly and easily, regular routine blood tests can help to screen patients at high risk of XDR-*A. baumannii* nosocomial infections for timely intervention to reduce the mortality and improve patient prognosis.

Moreover, NLR and cardiovascular diseases were significantly associated with mortality for patients with NSDs who had nosocomial infection with XDR-*A. baumannii*. It has been determined that the count of neutrophils is closely related to the CNS inflammation of NSDs and correlates with the severity of the illness.[40,41] Neutrophils are seen to increase and infiltrate brain tissue after intracerebral hemorrhage, and they also contribute to the inflammatory response through microglia.[42] In the meantime, lymphocytopenia plays a critical role in brain injury, which can lead to immunosuppression after hemorrhagic stroke.[43] In addition, a meta-analysis including 41 studies confirmed that an elevated NLR was associated with a 1.1- to 1.3-fold increased risk of a poor prognosis for stroke patients. Remarkably, cardiovascular disease and stroke are the leading causes of death and adult disability in China, and they share common risk factors and frequently coexist.[44] Typically, stroke causes neurovascular uncoupling, which disrupts the cerebral auto-regulation, thus making cerebral blood flow directly dependent on cardiac function. Myocardial injury, ischemia-like electrocardiographic changes, and arrhythmias are often seen in acute stroke patients, even when there is no underlying primary heart disease.[45] Bilt et al discovered that cardiac dysfunction is correlated with a higher risk of death, delayed cerebral ischemia, and a poor outcome after subarachnoid hemorrhage.[46] Further research is necessary to investigate whether the cardiac dysfunction is triggered by stroke or is the underlying cause of the stroke.

There are some limitations that should be acknowledged. Firstly, all patients in this study were treated in the same hospital, and the results of such a single-centre study might not apply to other medical settings. Moreover, this is a retrospective study, information was collected from medical records, which may not be completely accurate. Finally, it is difficult to accurately define whether certain diseases are underlying or complications.

Conclusion

XDR-*A. baumannii* nosocomial infections are a serious concern in patients suffering from NSDs with a high mortality. Hypertension, pulmonary infections, indwelling gastric tube, tracheotomy, bladder irrigation, and deep puncture were independent risk factors for XDR-*A. baumannii* nosocomial infections in patients with NSDs. The AST/ALT ratio, NLR, and pulmonary infections accounted for a higher risk of death in patients with XDR-*A. baumannii* nosocomial infections. NLR and cardiovascular diseases were reliable predictors for mortality of XDR-*A. baumannii* nosocomial infections among patients with NSDs. Understanding factors contributing to patient mortality is crucial for improving treatment strategies and outcomes.

Ethics Approval and Informed Consent

The study protocol was approved by the Institutional Review Board of the Affiliated Hospital of Southwest Medical University. The study was conducted in accordance with the Declaration of Helsinki, and all participants provided written informed consent.

Acknowledgments

The authors are grateful to the staff of the microbiology lab for their assistance in identifying bacteria and performing antimicrobial susceptibility testing.

Funding

This study was funded by the National College Students' Innovative Entrepreneurial Training Plan Program (202110632051).

Disclosure

The authors report no conflicts of interest in this work.

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