EVOLVING ANTIBIOTIC RESISTANCE PATTERNS OF CARBAPENEM-RESISTANT *ACINETOBACTER BAUMANNII* IN A SLOVAK TERTIARY INTERNAL MEDICINE DEPARTMENT: A THREE-YEAR ANALYSIS

Vývoj vzorcov antibiotickej rezistencie karbapenémrezistentného *Acinetobacter baumannii* na internej klinike univerzitnej nemocnice na Slovensku: trojročná analýza

Yashar JALALI

Faculty of Medicine, Comenius University in Bratislava, 5th Department of Internal Medicine, University Hospital Bratislava, Head of Department: prof. MUDr. J. Payer, MD., PhD., FRCP, FEFIM

Abstract
Introduction. *Acinetobacter baumannii* is a significant nosocomial pathogen known for its ability to acquire extensive drug resistance, particularly to carbapenems. This study aimed to evaluate the prevalence and antimicrobial resistance patterns of carbapenem-resistant *A. baumannii* (CRAB) over a three-year period in a tertiary care hospital.
Methods. We conducted a prospective observational study from January 2023 to September 2025, analyzing all clinically relevant *A. baumannii* isolates from patients hospitalized in internal medicine wards. Demographic data, site of infection, and antibiotic susceptibility profiles were collected. Resistance trends were assessed using Fisher's exact test and Cochran–Armitage trend analysis.
Results. A total of 65 *A. baumannii* isolates were identified, of which 41 (63%) were carbapenem-resistant. CRAB isolates exhibited 100% resistance to piperacillin–tazobactam, cephalosporins, aztreonam, and ciprofloxacin. High resistance to aminoglycosides and trimethoprim–sulfamethoxazole was observed, with minor, non-significant fluctuations. All isolates remained fully susceptible to colistin throughout the study.
Conclusion. The study highlights the persistent prevalence of extensively drug-resistant *A. baumannii*, with colistin as the only reliably active agent. These findings underscore the urgent need for ongoing resistance monitoring, antimicrobial stewardship, and targeted infection control strategies to preserve remaining treatment options (Tab. 1, Fig. 2, Ref. 14). Text in PDF www.lekarsky.herba.sk.
KEY WORDS: antibiotic resistance, *Acinetobacter baumannii,* carbapenem resistance, antibiotic resistance trends, antibiotic stewardship.
Lek Obz 2025, 74 (12): 452-456

Abstrakt
Úvod. *Acinetobacter baumannii* je významný nozokomiálny patogén známy svojou schopnosťou získavať rozsiahlu liekovú rezistenciu, najmä voči karbapenémom. Cieľom tejto štúdie bolo zhodnotiť prevalenciu a vzorce antimikrobiálnej rezistencie karbapeném-rezistentných kmeňov *A. baumannii* (CRAB) počas trojročného obdobia v prostredí terciárneho zdravotníckeho zariadenia.
Metodika. Od januára 2023 do septembra 2025 sme uskutočnili prospektívnu observačnú štúdiu, v rámci ktorej boli analyzované všetky klinicky významné izoláty *A. baumannii* od pacientov hospitalizovaných na oddeleniach internej medicíny. Zbierali sa demografické údaje, miesto infekcie a profily citlivosti na antibiotiká. Trendy rezistencie boli hodnotené pomocou Fisherovho exaktného testu a Cochran–Armitageho testu trendu.
Výsledky. Celkovo bolo identifikovaných 65 izolátov *A. baumannii*, z ktorých 41 (63 %) bolo rezistentných na karbapenémy. Izoláty CRAB vykazovali 100 % rezistenciu na piperacilín–tazobaktám, cefalosporíny, aztreonam a ciprofloxacín. Bola pozorovaná vysoká rezistencia na aminoglykozidy a trimetoprim–sulfametoxazol, s drobnými, štatisticky nevýznamnými výkyvmi. Všetky izoláty zostali počas celej štúdie plne citlivé na kolistín.
Záver. Štúdia poukazuje na pretrvávajúcu prevalenciu rozsiahlo rezistentného *A. baumannii*, pričom kolistín zostáva jediným spoľahlivo účinným liečivom. Tieto zistenia zdôrazňujú naliehavú potrebu kontinuálneho monitorovania rezistencie, racionálneho používania antibiotík a cielenej kontroly infekcií s cieľom zachovať zostávajúce terapeutické možnosti *(tab. 1, obr. 2, lit. 14). Text v PDF www.lekarsky.herba.sk.*
KĽÚČOVÉ SLOVÁ: antibiotická rezistencia, *Acinetobacter baumannii*, karbapenémová rezistencia, trendy antibiotickej rezistencie, antibiotická politika.
Lek Obz 2025, 74 (12): 452-456

Introduction

Acinetobacter baumannii is a Gram-negative, non-fermenting opportunistic pathogen frequently associated with hospital-acquired infections, particularly in intensive care units and among immunocompromised patients (1). Its ability to survive in harsh hospital environments and rapidly acquire antimicrobial resistance (AMR) has made it a significant threat to clinical care (1).

In recent years, *A. baumannii* has demonstrated increasing resistance to multiple antibiotic classes, including β-lactams, fluoroquinolones, and aminoglycosides (2). Of particular concern is the widespread emergence of CRAB, which are often resistant to nearly all available antibiotics (2, 3). In recognition of this threat, the World Health Organization has listed CRAB as a priority 1 (critical) pathogen requiring urgent research and intervention (4).

Multiple surveillance reports and international studies have confirmed a steady rise in resistance rates among CRAB isolates, with declining susceptibility even to last-resort agents such as tigecycline and colistin (5, 6). These trends pose a growing clinical challenge worldwide, leading to longer hospital stays, increased treatment costs, and poorer patient outcomes (6).

Given the high variability of resistance patterns between institutions and over time, continuous local surveillance is essential for guiding empirical treatment and optimizing antibiotic stewardship. This study presents a three-year analysis (2023–2025) of antibiotic susceptibility trends in CRAB isolates from our internal medicine department. The aim is to compare recent susceptibility trends with previously published four-year data (7) to evaluate potential shifts in resistance patterns over time and inform clinical decision-making.

Methods

In this observational, prospective, cross-sectional study, we monitored and gathered data from all clinically relevant isolates of *A. baumannii* from patients hospitalised in two standard male and female wards, an intermediary ward for critically ill patients with need of central monitoring and an intensive care unit of the fifth department of internal medicine of University Hospital Bratislava, Ružinov for a period of three years (from the beginning of 2023 to the end September 2025). For each isolate, we collected information on demographic data of patients, place of sampling, and antibiogram. There was no specific process for the selection of patients in this study. However, all patients included in the study had active infectious processes caused by *A. baumannii* with raised inflammatory markers. Patients with a prior history of colonisation with *A. baumannii* were excluded from the study. Sterile swabs were used to collect samples from the nose, tonsils, wounds, and decubitus. Blood sampling was performed via peripheral intravenous puncture. Urine was collected via mid-stream urine sampling or via urinary catheter. Samples were processed using conventional methods approved by the Slovak Ministry of Health. Strain identification was performed in accordance with classical isolation and classical biochemical and cultivation methods with a Bruker MALDI Biotyper (Bruker, Billerica, MA, USA), which uses the MALDI-TOF Mass Spectrometry method. Antibiotic testing results were interpreted according to EUCAST guidelines (European Committee on Antimicrobial Susceptibility Testing) (8). The panel of tested antibiotics was pre-determined by diagnostic laboratories, defined for Gram-negative isolates. Data collected during the monitoring period were analysed using Microsoft Excel. Data were analysed using descriptive and inferential statistical methods. Categorical variables representing antimicrobial susceptibility were expressed as absolute numbers and percentages. Differences in resistance rates between the first and last year of the observation period were evaluated using **Fisher's exact test**. To assess overall temporal changes across the three consecutive years, a **Cochran–Armitage trend test** was applied. A p-value of <0.05 was considered statistically significant. Extensively drug resistant (XDR) was defined as non-susceptibility to ≥1 agent in all but ≤2 antimicrobial categories. Ethical review and approval were not required for the study (as an observational study) on human participants in accordance with local legislation and institutional requirements. Written informed consent for participation was not required for this study in accordance with national legislation and the institutional requirements.

Results

A total of 65 samples of *A. baumannii* were isolated. Four samples were isolated from patients hospitalised in intensive care unit (ICU) (4/65, 6%), 10 samples were isolated from patients hospitalised in intermediary ward for critically ill patients (10/65, 15%) and 51 samples were isolated from patients hospitalised in standard male and female wards (51/65, 79%) during study period. Average hospitalisation in ICU was recorded six to eight days, and in other wards 25 days. Male patients were more likely to be infected by *A. baumannii* than female patients (54% to 46%). The mean age of male patients was approximately 10 years higher than that of female patients (Tab. 1).

Carbapenem resistant *A. baumannii* was predominantly isolated from respiratory secretions (n/N: 17/41, 41%), followed by wounds or decubitus samples (n/N: 14/41, 34%), urinary tract infections (n/N: 6/41, 15%), haemocultures, and samples from central venous catheter-related infections (n/N: 4/41, 10%) (Fig. 1).

A susceptibility test was performed on the panel of 19 antibiotics from seven antibiotic families as the routine antibiogram examination on the bacterium. The antibiotic families included penicillins (ampicillin-sulbactam, and piperacillin-tazobactam), cephalosporines (cefotaxime, ceftazidime, cefepime, and cefoperazone-sulbactam), carbapenems (imipenem, and meropenem), monobactams (aztreonam), fluroquinolones (ciprofloxacin), aminoglycosides (amikacin, gentamicin, and tobra-

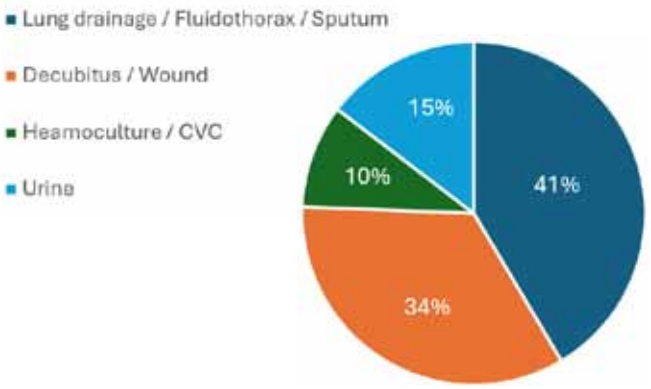
mycin), sulphonamides, (trimethoprim-sulfamethoxazole), and polymyxins (colistin).

Table 1. Demographic data of isolated *A. baumannii*.

	Total	2023	2024	2025
Number of isolated *A. baumannii*	65	30	19	16
Number of isolated CR A. baumannii	41/65, 63%	22/30, 73%	10/19, 53%	9/16, 56%
Number of male patients (n/N, cases %)	35/65, 54%			
Age of male patients (Mean)	71.8 (SD ±15.3)			
Number of female patients (n/N, cases %)	30/65, 46%			
Age of female patients (Mean)	62.3 (SD ±19.1)			
Hospitalization duration (Av. days)	25.7			

Av.: average, CR: carbapenem resistant, N: total number of isolated samples, n: number of isolated samples for given variable, SD: standard deviation.

Figure 1. Frequency of isolation (%) of carbapenem resistant *A. baumannii* from a given site.



Three years of antibiotic resistance trends for isolated CRABs are shown in Figure 2 three columns are displayed above each tested antibiotic, with each representing a year from 2023 to 2025. Accumulated percentage of susceptibility (in blue) is shown in contrast to accumulated percentage of resistance (in orange) to a given antibiotic in a given year for each column. Rationally data on resistance to imipenem and meropenem are not shown in the figure, as all included isolates were by default CR.

All isolated strains of *CRAB* demonstrated 100% resistance to piperacillin–tazobactam, all tested cephalosporins, aztreonam, and ciprofloxacin throughout the study period (Figure 2). Susceptibility to trimethoprim and amikacin was observed in only one isolate in 2023, while all isolates collected in 2024 and 2025 were fully resistant to these agents. Notably, resistance to ampicillin–sulbactam, tobramycin, and gentamicin showed a slight decreasing trend from 2023 to 2025, although all isolates in 2024 exhibited complete resistance to gentamicin. The significance of changes in resistance trends between 2023 and 2025 was determined using Fisher's exact test, while temporal changes across all three years were examined using the Cochran–Armitage trend test. Neither test demonstrated statistically significant changes in resistance trends for any of the three antibiotics (ampicillin–sulbactam: Fisher's exact test, p = 1.000, odds ratio (OR) = 1.29; Cochran–Armitage, p = 0.808; tobramycin: Fisher's exact test, p = 0.503, OR = 2.63; Cochran–Armitage, p = 0.512; gentamicin: Fisher's exact test, p = 0.195, OR = 6.00; Cochran–Armitage, p = 0.178). Resistance to colistin consistently remained at 0% for all isolates during the entire study period.

Discussion

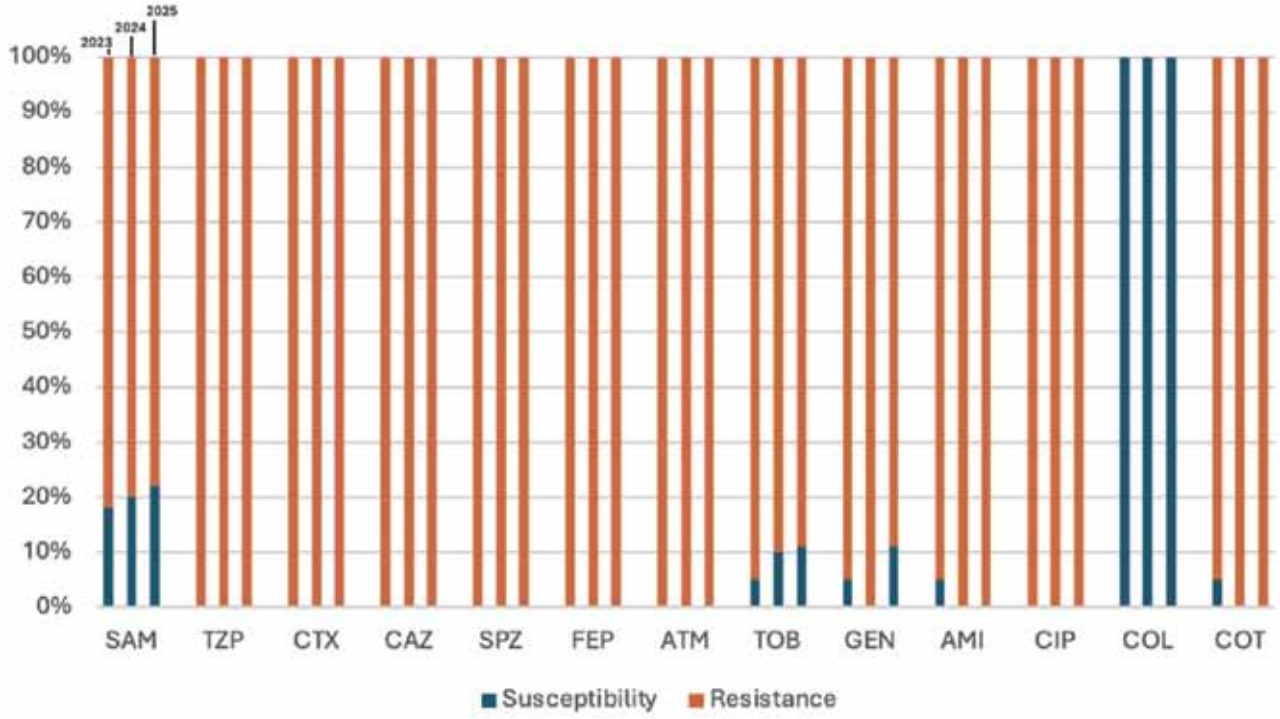
In our three-year observational study, we identified 65 isolates of *Acinetobacter baumannii*, of which 41 (63%) were CRAB. This proportion reflects the ongoing global threat posed by multidrug-resistant *A. baumannii* in healthcare settings, particularly in internal medicine and critical care units (9). Male patients accounted for a slight majority of cases (54%), and the mean age among male patients was approximately a decade higher than that of female patients. This difference may contribute to the gender imbalance observed, as older patients are more susceptible to invasive procedures, prolonged hospital stays, and immune system decline, all of which increase the risk of infection.

The resistance profiles in our cohort illustrate the entrenched nature of CRAB in the clinical environment. All isolates were uniformly resistant to piperacillin–tazobactam, all tested cephalosporins, aztreonam, and ciprofloxacin across all three years. This multidrug resistance is consistent with the action of OXA-type carbapenemases and extended-spectrum β-lactamases, which confer cross-resistance to nearly all β-lactam antibiotics, including carbapenems and third-generation cephalosporins (10).

High levels of resistance were also observed to aminoglycosides (amikacin, gentamicin, tobramycin), trimethoprim–sulfamethoxazole, and ampicillin–sulbactam. Although minor fluctuations were noted over time, particularly a slight decline in gentamicin and tobramycin resistance in 2025, none of these changes reached statistical significance (ampicillin-sulbactam: p = 1.000, OR = 1.29; tobramycin: p = 0.503, OR = 2.63; gentamycin: p = 0.195, OR = 6.00). This suggests the persistence of XDR under continued selective pressure, a pattern the echoed as well in regional studies across the Middle East and Asia (11,12).

Importantly, all CRAB isolates in our study remained fully susceptible to colistin throughout the three-year period. This observation is in line with our previously published four-year report from similar settings where colistin remains one of the last effective options against XDR *A. baumannii* (7). However, the reliability of colistin is increasingly uncertain. A multinational surveillance study from Europe reported resistance in nearly half (47.7%) of CRAB isolates from ventilator-associated

Figure 2. Three-year trends of antibiotic resistance in isolated CR strains of *A. baumannii*.



AMI: amikacin, ATM: aztreonam, CAZ: ceftazidime, CIP: ciprofloxacin, COL: colistin, COT: co-trimoxazole (trimethoprim-sulfamethoxazole), CTX: cefotaxime, FEP: cefepime, GEN: gentamycin, SAM: ampicillin-sulbactam, SPZ: sulperazone (cefoperazone-sulbactam), TOB: tobramycin, TZP: tazocin (piperacillin-tazobactam).

pneumonia (13), signaling the potential emergence of pan-drug resistant strains. As colistin remains a last-resort agent, its preserved effectiveness emphasizes the critical need for stringent antimicrobial stewardship. Although combination therapy involving colistin and carbapenems has been proposed, recent meta-analyses suggest no significant advantage over colistin monotherapy in reducing mortality or improving clinical outcomes, challenging previous assumptions about synergistic benefit (14).

Taken together, our data reflect a typical and concerning resistance profile for CRAB in modern clinical practice—dominated by XDR phenotypes, sustained by selective pressure, and vulnerable to losing colistin as a viable treatment option. Although this study was not designed to determine whether isolates represented true healthcare-associated infections or colonization, and no molecular typing was performed, the findings still offer meaningful insight into antimicrobial resistance trends in a high-risk clinical population.

These results highlight the critical need for continued surveillance and aggressive antimicrobial stewardship. This includes strict regulation of empiric antibiotic use, especially carbapenems and aminoglycosides, regular updates to hospital antibiograms, and implementation of infection control measures tailored to high-risk wards. Preserving the efficacy of last-line agents like colistin will depend on coordinated efforts to limit overuse and prevent the spread of resistant strains within healthcare institutions.

Conclusion

Our study reinforces the growing concern surrounding the persistence and spread of extensively drug-resistant *Acinetobacter baumannii* in clinical settings, particularly in vulnerable patient populations. The high prevalence of CRAB, its consistent resistance to multiple antibiotic classes, and the sustained susceptibility to colistin underscore both the severity of the threat and the narrowing window of effective treatment options. These findings emphasize the urgency of implementing targeted antimicrobial stewardship, infection prevention strategies, and ongoing resistance surveillance to mitigate the clinical and public health impact of this formidable pathogen.*

*__Compliance with Ethics Requirements:__ Authors declare no conflict of interest regarding this article. The authors declare, that all the procedures and experiments of this research respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008 (5), as well as the national law.

Conflict of interest: The authors declare no conflict of interest.

References

1. MA C, McCLEAN S. Mapping Global Prevalence of Acinetobacter baumannii and Recent Vaccine Development to Tackle It. Vaccines (Basel) 2021, 9. Doi 10.3390/vaccines9060570.
2. ASSIMAKOPOULOS SF, KARAMOUZOS V, ELEFTHERIOTIS G, LAGADINOU M, BARTZAVALI C, KOLONITSIOU F, PALIOGIANNI

F, FLIGOU F, MARANGOS M. Efficacy of Fosfomycin-Containing Regimens for Treatment of Bacteremia Due to Pan-Drug Resistant Acinetobacter baumannii in Critically Ill Patients: A Case Series Study. Pathogens 2023, 12: 286.
3. MANCUSO G, MIDIRI A, GERACE E, BIONDO C. Bacterial Antibiotic Resistance: The Most Critical Pathogens. Pathogens 2021, 10. Doi 10.3390/pathogens10101310.
4. NOVOVIĆ K, JOVČIĆ B. Colistin Resistance in Acinetobacter baumannii: Molecular Mechanisms and Epidemiology. Antibiotics 2023, 12, 516.
5. KO SY, KIM N, PARK SY, KIM SY, SHIN M, LEE JC. Acinetobacter baumannii under Acidic Conditions Induces Colistin Resistance through PmrAB Activation and Lipid A Modification. Antibiotics (Basel) 2023, 12. Doi 10.3390/antibiotics12050813.
6. AYOBAMI O, WILLRICH N, HARDER T, OKEKE IN, ECKMANNS T, MARKWART R. The incidence and prevalence of hospital--acquired (carbapenem-resistant) Acinetobacter baumannii in Europe, Eastern Mediterranean and Africa: a systematic review and meta-analysis. Emerg Microbes Infect 2019, 8: 1747-1759. Doi 10.1080/22221751.2019.1698273.
7. JALALI Y, LIPTÁKOVÁ A, JALALI M, PAYER J. Moving toward Extensively Drug-Resistant: Four-Year Antimicrobial Resistance Trends of Acinetobacter baumannii from the Largest Department of Internal Medicine in Slovakia. Antibiotics 2023, 12: 1200.
8. TESTING, E.c.o.a.s. Clinical breakpoints - breakpoints and guidance. EUCAST 2023, January 2, 2023.
9. MÜLLER C, REUTER S, WILLE J, XANTHOPOULOU K, STEFANIK D, GRUNDMANN H, HIGGINS P, SEIFERT H. A global view on carbapenem-resistant Acinetobacter baumannii. mBio 2023, 14. Doi 10.1128/mbio.02260-23.
10. NOVOVIĆ K, JOVČIĆ B. Colistin Resistance in Acinetobacter baumannii: Molecular Mechanisms and Epidemiology. Antibiotics 2023, 12. Doi 10.3390/antibiotics12030516.
11. LEUNGTONGKUM U. Dissemination of class D carbapenemase resistance genes and plasmid profiles of Acinetobacter baumannii isolated from Chiangrai Prachanukroh hospital, Thailand. NU. International Journal of Science 2016, 13: 11-23.
12. BEIGVERDI R, SATTARI-MARAJI A, EMANEINI M, JABALAMELI F. Status of carbapenem-resistant Acinetobacter baumannii harboring carbapenemase: First systematic review and meta-analysis from Iran. Infection, genetics and evolution: Journal of molecular epidemiology and evolutionary genetics in infectious diseases 2019, 73: 433-443. Doi 10.1016/j.meegid.2019.06.008.
13. NOWAK J, ZANDER E, STEFANIK D, HIGGINS PG, ROCA I, VILA J, McCONNELL MJ, CISNEROS JM, SEIFERT H, WP4, MWG. High incidence of pandrug-resistant Acinetobacter baumannii isolates collected from patients with ventilator-associated pneumonia in Greece, Italy and Spain as part of the MagicBullet clinical trial. Journal of Antimicrobial Chemotherapy 2017, 72: 3277-3282. Doi 10.1093/jac/dkx322.
14. HUANG C, CHEN I, TANG T. Colistin Monotherapy versus Colistin plus Meropenem Combination Therapy for the Treatment of Multidrug-Resistant Acinetobacter baumannii Infection: A Meta-Analysis. Journal of Clinical Medicine 2022, 11: 3239.

Accepted for publication Oct 27, 2025.

Address for communication:
MUDr. Yashar JALALI
5th Department of Internal Medicine
Ružinovská 4810/6
821 01 Bratislava
Slovakia
E-mail: *yashar.jalali@fmed.uniba.sk*