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ABSTRACT

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CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS OF INFECTIONS CAUSED BY ACINETOBACTER BAUMANNII IN INTENSIVE CARE UNIT PATIENTS

Introduction. *Acinetobacter baumannii* is one of the leading causative agents of nosocomial infections in intensive care units, particularly in patients with COVID-19. The global spread of multidrug-resistant strains of this pathogen poses a critical threat to public health. The World Health Organization has included carbapenem-resistant strains of *A. baumannii* in the list of bacteria of critical priority. The COVID-19 pandemic has significantly worsened the epidemiological situation by creating favorable conditions for the development of secondary bacterial infections through prolonged hospitalization, invasive procedures, and immunosuppression.

Aim. To evaluate the prevalence, clinical features, antibiotic resistance profile, and treatment outcomes of *A. baumannii* infections in COVID-19 patients in the intensive care unit.

Materials and methods. A study of 50 cases of *A. baumannii* infection in COVID-19 patients in the ICU during 2020–2022 was conducted. Microbiological diagnostics were performed with determination of antibiotic susceptibility using disk diffusion and microdilution methods according to EUCAST. Molecular genetic analysis was performed using the BIO-RAD CFX96 Real-Time PCR system with the RevoDx Sepsis Pathogen Detection Kit to detect carbapenemase genes.

Results. The mean age of patients was 56.3 ± 12.5 years, 62% were male. The most common infection sites were ventilator-associated pneumonia – 40%, sepsis – 40%, and catheter-associated urinary tract infections – 20%. High levels of resistance to carbapenems (62%), fluoroquinolones (75%), and third- and fourth-generation cephalosporins (85%) were detected. Colistin retained the highest activity (92% susceptible isolates), tigecycline showed moderate efficacy (74%). Among resistance genes, bla_{OXA-23} (65%), bla_{NDM} (25%), and bla_{VIM} (12%) dominated. Combination therapy with colistin plus tigecycline provided

78% survival compared to 42% with carbapenem monotherapy. Overall mortality was 36%.

Discussion. The obtained results are consistent with European data on high levels of carbapenem resistance in the Eastern European region. Molecular genetic analysis confirmed the dominance of the bla_{OXA-23} gene, characteristic of this region. Detection of metallo-β-lactamase genes (bla_{NDM}, bla_{VIM}) was associated with worse prognosis and lower patient survival. The advantage of combination therapy over monotherapy confirms international recommendations for the treatment of infections caused by multidrug-resistant gram-negative pathogens.

Conclusions. *A. baumannii* is one of the most dangerous nosocomial pathogens in ICU with high levels of multidrug resistance. Combination antibiotic therapy is associated with better clinical outcomes. Strengthening infection control and antimicrobial stewardship programs is necessary.

Keywords: *Acinetobacter baumannii*, drug resistance bacterial, carbapenemases, colistin, tigecycline, pneumonia ventilator-associated, sepsis, COVID-19, molecular epidemiology, antimicrobial stewardship.

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КЛІНІКО-ЕПІДЕМІОЛОГІЧНІ ОСОБЛИВОСТІ ІНФЕКЦІЙ, СПРИЧИНЕНИХ ACINETOBACTER BAUMANNII, У ПАЦІЄНТІВ ВІДДІЛЕННЯ ІНТЕНСИВНОЇ ТЕРАПІЇ

Вступ. *Acinetobacter baumannii* є одним із провідних збудників нозокоміальних інфекцій у відділеннях інтенсивної терапії (ВІТ), особливо у пацієнтів з COVID-19. Глобальне поширення мультирезистентних штамів цього патогена становить критичну загрозу для громадського здоров'я. Всесвітня організація охорони здоров'я включила карбапенем-резистентні штами *A. baumannii* до переліку бактерій критичного пріоритету. Пандемія COVID-19 значно погіршила епідеміологічну ситуацію, створивши сприятливі умови для розвитку вторинних бактеріальних інфекцій через тривалу госпіталізацію, інвазивні процедури та імуносупресію.

Мета. Оцінити поширеність, клінічні особливості перебігу, профіль антибіотикорезистентності та результати лікування інфекцій, спричинених *A. baumannii*, у пацієнтів з COVID-19 у відділенні інтенсивної терапії.

Матеріали та методи. Проведено дослідження 50 випадків інфекції *A. baumannii* у пацієнтів з COVID-19 у ВІТ протягом 2020–2022 років. Виконано мікробіологічну діагностику з визначенням антибіотикочутливості методами диск-дифузії та мікророзведень згідно з EUCAST. Молекулярно-генетичний аналіз проводили за допомогою системи BIO-RAD CFX96 Real-Time PCR з набором RevoDx Sepsis Pathogen Detection Kit для виявлення генів карбапенемаз.

Результати. Середній вік пацієнтів становив 56,3 ± 12,5 років, 62% були чоловіками. Найчастішими локалізаціями інфекції були вентилятор-асоційована пневмонія (40%), сепсис (40%) та інфекції сечовивідних шляхів (20%). Виявлено високий рівень резистентності до карбапенемів (62%), фторхінолонів (75%) та цефалоспоринів III–IV покоління (85%). Колістин зберігав найвищу активність (92%

чутливих ізолятів), тигециклін демонстрував помірну ефективність (74%). Серед генів резистентності домінували bla_{OXA-23} (65%), bla_{NDM} (25%) та bla_{VIM} (12%). Комбінована терапія колістин плюс тигециклін забезпечила виживаність 78% порівняно з 42% при монотерапії карбапенемами. Загальна летальність становила 36%.

Обговорення. Отримані результати узгоджуються з європейськими даними щодо високого рівня карбапенем-резистентності в Східноєвропейському регіоні. Молекулярно-генетичний аналіз підтвердив домінування гена bla_{OXA-23}, характерного для цього регіону. Виявлення генів метало-β-лактамаз (bla_{NDM}, bla_{VIM}) асоціювалося з гіршим прогнозом та нижчою виживаністю пацієнтів. Перевага комбінованої терапії над монотерапією підтверджує міжнародні рекомендації щодо лікування інфекцій, спричинених мультирезистентними грамнегативними патогенами.

Висновки. *A. baumannii* є одним із найнебезпечніших нозокоміальних патогенів у ВІТ з високим рівнем мультирезистентності. Комбінована антибіотикотерапія асоціюється з кращими клінічними результатами. Необхідне посилення програм інфекційного контролю та антимікробного стюардшипу.

Ключові слова: *Acinetobacter baumannii*, антибіотикорезистентність, карбапенемази, колістин, тигециклін, вентилятор-асоційована пневмонія, сепсис, COVID-19, молекулярна епідеміологія, антимікробний стюардшип.

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ABBREVIATIONS

CAUTI – catheter-associated urinary tract infections
CDC – Centers for Disease Control and Prevention
CLSI – Clinical and Laboratory Standards Institute
ECDC – European Centre for Disease Prevention and Control
EUCAST – European Committee on Antimicrobial Susceptibility Testing
ICMJE – International Committee of Medical Journal Editors
ICU – intensive care unit
IDSA – Infectious Diseases Society of America
MBL – metallo-β-lactamases
MDR – multidrug-resistant
MIC – minimum inhibitory concentration
MV – mechanical ventilation
PCR – polymerase chain reaction
PDR – pandrug-resistant
VAP – ventilator-associated pneumonia
WHO – World Health Organisation
XDR – extensively drug-resistant

INTRODUCTION

Acinetobacter baumannii represents one of the leading aetiological agents of nosocomial infections, posing a particular threat to patients in intensive care units (ICUs). This Gram-negative coccobacillary microorganism is characterised by a unique ability to survive in adverse environmental conditions for extended periods – from several days to several weeks on dry surfaces, medical equipment, and care items. This feature makes *A. baumannii* an ideal nosocomial pathogen capable of persisting in the hospital environment and causing outbreaks in intensive care units [1–2].

The global spread of multidrug-resistant (MDR) strains of *A. baumannii* has become one of the most serious problems in modern medicine and global health. In 2017, the World Health Organisation (WHO) included carbapenem-resistant strains of *A. baumannii* in the list of bacteria of critical priority (Priority 1: CRITICAL), for which the development of new antibiotics is urgently needed [1]. The US Centres for Disease Control and Prevention (CDC) in its report "Antibiotic Resistance Threats in the United States, 2019" classified carbapenem-resistant *A. baumannii* as an urgent threat to public health, estimating approximately 8,500 annual cases in the USA with approximately 700 fatalities [2].

The European Centre for Disease Prevention and Control (ECDC) in its annual report on antimicrobial resistance surveillance in Europe (2023, data for 2022) reported a continued increase in the frequency of carbapenem-resistant strains of *A. baumannii* in European countries [3]. Analysis of data from 30 European Union and European Economic Area countries showed significant geographical variability: in Northern European countries (Norway, Sweden, Denmark, Netherlands), the level of carbapenem resistance remains low (less than 10 %), whilst in Southern and Eastern European countries (Greece, Italy, Romania, Bulgaria), this indicator often exceeds 60–70 %, and in some centres reaches 80–90 % [3].

In Ukraine, as in other Eastern European countries, there is a persistent trend towards an increase in the frequency of isolation of resistant strains of this microorganism. According to the National Centre for Public Health of Ukraine, the level of resistance of *A. baumannii* to carbapenems in 2023 was 60–65 %, which corresponds to average European indicators, whilst resistance to fluoroquinolones is higher and characteristic of Ukraine [4].

During the COVID-19 pandemic, which began at the end of 2019 and peaked in 2020–2021, *A. baumannii* infections posed a particular threat. Patients with severe coronavirus disease had an increased risk of developing bacterial complications, particularly those caused by Gram-negative multidrug-resistant pathogens, including *A. baumannii*. Studies conducted in various countries showed a significant increase in the frequency of nosocomial infections caused by A. baumannii amongst COVID-19 patients in ICUs [5–6].

Study aim – to evaluate the prevalence, clinical features, antibiotic resistance profile, and treatment outcomes of *Acinetobacter* infection in COVID-19 patients in the intensive care unit to optimise therapeutic approaches and improve clinical outcomes.

MATERIALS AND METHODS

A single-centre study was conducted of 50 clinical cases of infection caused by *A. baumannii* in COVID-19 patients. These cases were observed in the intensive care unit of the Kharkiv Regional Clinical Infectious Diseases Hospital during 2020–2022. The study was approved by the Ethics and Bioethics Commission of Kharkiv National Medical University, protocol №5 from 06.05.2026, and informed consent was obtained from all patients where possible.

Inclusion criteria: age from 18 years, confirmed diagnosis of COVID-19 by RT-PCR test, microbiologically verified *A. baumannii* infection, hospitalisation duration of at least 7 days, availability of complete clinical data. Exclusion criteria: unavailability of complete clinical data and presence of concomitant co-infections with other bacterial pathogens that could significantly complicate interpretation of treatment results. Diagnosis of nosocomial infection was established according to CDC [2] and ECDC [3] criteria.

Bacterial isolates of *A. baumannii* were isolated from various clinical materials: tracheal aspirate, sputum, bronchoalveolar lavage, blood, and urine. Identification of microorganisms was performed using a combination of methods: standard biochemical tests and molecular identification by PCR with determination of the $bla_{OXA\text{-}51\text{-}like}$ gene, which is a natural chromosomal gene present in all strains of *A. baumannii* and serves as a species-specific marker.

Determination of antibiotic susceptibility was performed by two phenotypic methods according to international standards: disc diffusion method on Mueller-Hinton agar and serial microdilution method in broth for determination of minimum inhibitory concentrations (MIC), according to EUCAST recommendations [7]. *Pseudomonas aeruginosa* ATCC 27853 and *Escherichia coli* ATCC 25922 were used as quality control strains.

Susceptibility to a wide spectrum of antibacterial drugs was tested, including carbapenems, fluoroquinolones, cephalosporins, aminoglycosides, colistin, and tigecycline. Results should be interpreted cautiously, as EUCAST/CLSI have not established clinical breakpoints for tigecycline against *A. baumannii*.

MDR strains were defined as resistant to at least one drug in three or more antibiotic classes. Extensively drug-resistant (XDR) strains were susceptible to only one or two classes of antibacterial agents [8].

For molecular genetic analysis, patient blood samples were examined using the BIO-RAD CFX96 Real-Time PCR system and the commercial RevoDx Sepsis Pathogen Detection Kit. This approach allowed qualitative detection and identification of nucleic acids of bloodstream infection pathogens, including *A. baumannii*, as well as determination of antibiotic resistance genes.

For *A. baumannii*, primary attention was paid to detecting carbapenemase genes: class D carbapenemases

(oxacillinases): *bla*$_{OXA-23}$, *bla*$_{OXA-24}$, *bla*$_{OXA-48}$, *bla*$_{OXA-58}$; MBL: *bla*$_{NDM}$, *bla*$_{VIM}$, *bla*$_{IMP}$; class A carbapenemases: *bla*$_{KPC}$; species-specific marker: *bla*$_{OXA-51-like}$ (natural for *A. baumannii*).

Collection of clinical data included: demographic characteristics, comorbidities, severity of condition according to APACHE II scale, localisation of infectious process, antibiotic therapy regimens, treatment duration, and clinical outcomes.

Statistical processing of data was performed using R software (version 4.x) and RStudio, as well as Microsoft Excel. Quantitative indicators were presented as M ± SD or median with interquartile range. Qualitative indicators were described by absolute and relative frequencies. The χ^2 Pearson test, Fisher's exact test, and Mann-Whitney test were used for group comparison. The critical level of significance for statistical hypothesis testing in this study was taken as 0.05.

RESULTS

The study included 50 patients with a mean age of 56.3 ± 12.5 years (range 22–78 years). Males predominated, comprising 62 % (n = 31), whilst females accounted for 38 % (n = 19). The mean duration of hospitalisation before infection development was 14.2 ± 8.7 days.

The severity of patients' condition according to the APACHE II scale at ICU admission averaged 18.4 ± 6.2 points. A significant proportion of patients received invasive medical procedures: mechanical ventilation was used in 68 % (n = 34) of patients, 92 % (n = 46) had a central venous catheter, and 96 % (n = 48) had a urinary catheter. The distribution of major comorbidities among the study population is illustrated in Figure 1.

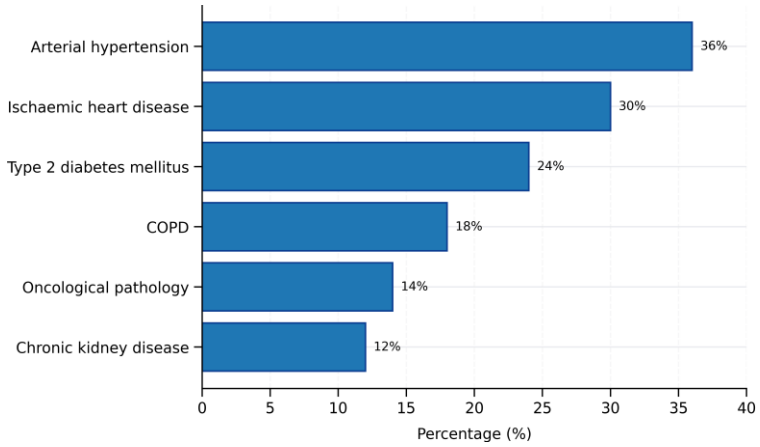

Figure 1. Prevalence of comorbidities among patients

A. baumannii most frequently caused the following clinical forms of infections:

– Ventilator-associated pneumonia (VAP) was diagnosed in 40 % (n = 20) of patients. The mean time of VAP development after intubation was 8.3 ± 4.2 days.

– Sepsis caused by *A. baumannii* was diagnosed in 40 % (n = 20) of patients. *A. baumannii* was isolated from blood in 100 % of sepsis cases; 60 % showed signs of multiple organ failure.

– Urinary tract infections were diagnosed in 20 % (n = 10) of patients. All cases were catheter-associated urinary tract infections (CAUTI).

Analysis of antibiotic susceptibility demonstrated a high level of resistance of A. baumannii to multiple classes of antibiotics, as illustrated in Figure 2.

The highest activity was demonstrated by: colistin – 92 % susceptible isolates; tigecycline – 74 % susceptible isolates (results should be interpreted cautiously, as EUCAST/CLSI have not established clinical breakpoints for tigecycline against *A. baumannii*).

Overall, 88 % (n = 44) of isolates were found to be MDR. XDR isolates accounted for 12 % (n = 6). One isolate (2 %) was PDR. Molecular analysis revealed widespread presence of intrinsic and acquired carbapenem resistance genes in patient samples, as shown in Figure 3 [9].

It should be noted that the RevoDx panel also detects ESBL genes (*bla*$_{TEM}$, *bla*$_{SHV}$, *bla*$_{CTX-M}$), which were identified in some samples. However, for *A. baumannii*, these genes are not determinants; their presence is characteristic mainly of Enterobacterales, whilst in *A. baumannii*, the key role is played by *bla*$_{OXA-23}$, *bla*$_{OXA-24/40}$, *bla*$_{OXA-58}$, *bla*$_{NDM}$, *bla*$_{VIM}$, *bla*$_{IMP}$ [10–11]. A combination of several resistance genes was observed in 40% of samples, which correlated with the phenotype of XDR and PDR.

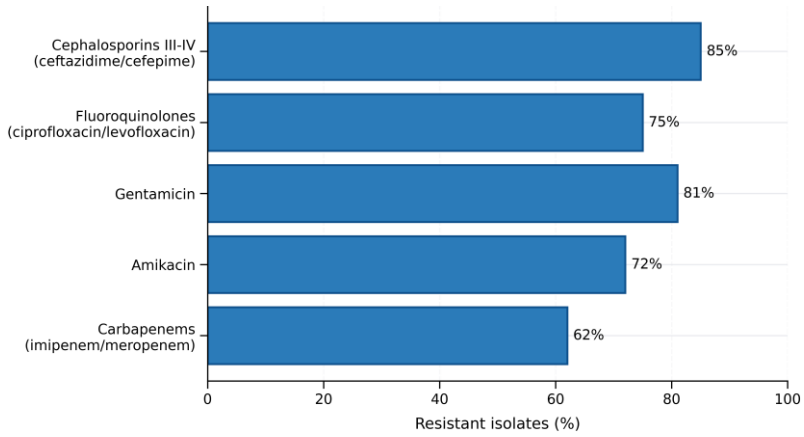

Figure 2. Antibiotic resistance profile of A. baumannii isolates

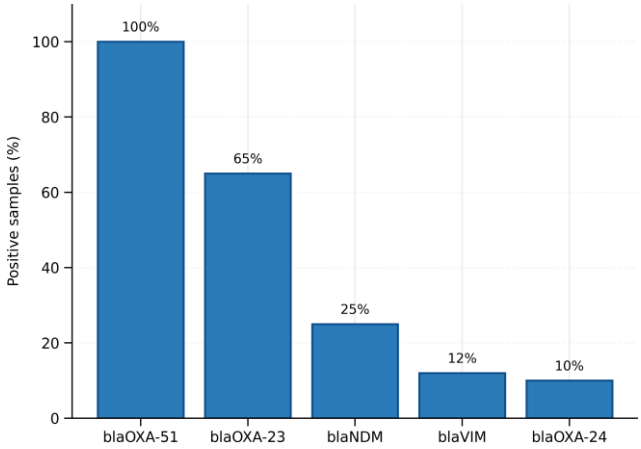

Figure 3. Distribution of carbapenem resistance genes in A. baumannii

Empirical antibiotic therapy was initiated on average 6.8 ± 3.2 hours after establishing the clinical diagnosis of infection. Targeted therapy was prescribed immediately after receiving antibiogram results (on days 3–4 from the moment of material collection).

Table 2. Risk factors associated with fatal outcome in patients with A. baumannii infection

Risk factor	OR	95% CI	p-value
Age >65 years	3.2	1.1–9.4	0.03
Sepsis	4.1	1.3–12.8	0.01
PDR	5.7	1.1–29.2	0.04
Delay of adequate therapy >48 h	2.8	1.0–7.9	0.049

***Abbreviations:* OR** *– Odds ratios,* **CI** *– confidence intervals,* **PDR** *– pandrug-resistant*

Distribution of therapy types: monotherapy was received by 44 % (n = 22) of patients (carbapenems – 12, colistin – 7, tigecycline – 3); combination therapy was prescribed to 56 % (n = 28) of patients (colistin plus tigecycline (n = 14), colistin plus carbapenem (n = 9), tigecycline plus carbapenem (n = 5)).

Combination therapy with colistin plus tigecycline provided the highest survival rate – 78 % (11 out of 14 patients recovered). Carbapenem monotherapy proved least effective with a survival rate of 42 % (5 out of 12 patients).

Overall mortality was 36 % (n = 18). Recovery with discharge was observed in 64 % of patients (n = 32). The mean duration of hospitalisation in patients who recovered was 28.4 ± 12.6 days.

Several factors were identified as being significantly associated with a fatal outcome, including advanced age, presence of sepsis, pandrug resistance of the pathogen, and delayed initiation of adequate therapy (Table 1).

Analysis of the relationship between the presence of resistance genes and clinical outcomes showed a clear correlation between genotype and patient prognosis. In our sample, patients with isolates carrying MBL genes (bla_{NDM} and bla_{VIM}) had lower survival: 25 % for bla_{NDM} (3 out of 12 patients) and 17 % for bla_{VIM} (1 out of 6 patients). These genes provide resistance to virtually all

β-lactam antibiotics and often coexist with other resistance mechanisms, creating strains with XDR or PDR profiles.

In patients with isolates having only the natural bla_{OXA-51} gene without additional acquired resistance determinants, survival was 80 %. These data emphasise the critical importance of molecular genetic testing for predicting clinical outcomes and early detection of highly resistant strains.

DISCUSSION

The results of our study confirm the global trend towards the spread of multidrug-resistant strains of *A. baumannii* in ICU, particularly in the context of the COVID-19 pandemic. The resistance profile observed in this study corresponds to the epidemiological situation reported in European and national surveillance data, confirming the widespread circulation of carbapenem-resistant *Acinetobacter baumannii* in the region [3,4].

The microorganism rapidly acquires antibiotic resistance through several mechanisms: production of β-lactamases (including carbapenemases), modification of penicillin-binding proteins, changes in outer membrane porins, active efflux pumps, and modification of antibiotic binding sites. Effective transfer of resistance genes occurs horizontally through plasmids, transposons, and integrons, promoting rapid spread of resistance in bacterial populations. Formation of biofilms on medical equipment (endotracheal tubes, central venous catheters, urinary catheters) provides additional protection from antibiotics and disinfectants, significantly complicating eradication of the microorganism [10–11].

Molecular mechanisms of *A. baumannii* resistance to carbapenems are primarily associated with production of carbapenemases – enzymes capable of hydrolysing the β-lactam ring of carbapenems, rendering these antibiotics ineffective [10]. According to Ambler classification, carbapenemases are divided into four classes (A, B, C, D) depending on the structure of the active centre. For *A. baumannii*, the greatest clinical significance is held by class B enzymes (MBL) and class D (oxacillinases) [10–11].

Class D oxacillinases (OXA-type) are the most common carbapenemases in *A. baumannii*. The *blaOXA-51-like* gene is a natural chromosomal gene present in all strains of *A. baumannii* and serves as a species-specific marker for identification of this species. However, by itself, it usually does not provide clinically significant resistance to carbapenems unless its expression is enhanced by insertion sequences (e.g., ISAba1) [11]. Acquired carbapenemase genes include *blaOXA-23*, *blaOXA-24/40*, *blaOXA-58*, *blaOXA-143*, and others. Amongst them, *blaOXA-23* is the most widespread globally and is associated with epidemic clones of *A. baumannii* that have spread worldwide [11–12].

MBL (class B) include enzymes of the *NDM* (New Delhi metallo-β-lactamase), *VIM* (Verona integron-encoded metallo-β-lactamase), *IMP* (imipenemase), and other families. Unlike oxacillinases, MBLs contain zinc ions in their active centre and are capable of hydrolysing virtually all β-lactam antibiotics, including carbapenems, but not monobactams (aztreonam). A particular danger is that MBL genes are often located on mobile genetic elements (plasmids, transposons, integrons) and are easily transferred between different bacterial species horizontally [8, 10–11].

Comparative analysis with data from other countries shows that the level of carbapenem resistance of *A. baumannii* varies significantly geographically. In Northern European countries (Scandinavia, Netherlands, Germany), this indicator remains relatively low (10–25 %) due to strict infection control protocols, limited use of carbapenems, and active antimicrobial stewardship programmes [3]. Whilst in Southern and Eastern European countries (Greece, Italy, Romania, Bulgaria, Balkan region countries), this indicator often exceeds 60–80 % [3, 12]. Our results reflect the epidemiological situation characteristic of the Eastern European region.

Colistin retains the highest activity against *A. baumannii* with a susceptibility level of over 90% according to EUCAST recommendations [7], confirming its significance as a "last-line" drug. However, the emergence of cases of resistance to colistin worldwide, associated with mechanisms of lipopolysaccharide modification of the cell wall, requires vigilant monitoring [13]. Tigecycline demonstrates moderate efficacy (60–75 %) and, according to IDSA [14] and ECDC [3] recommendations, is most effective as part of combination regimens but is not recommended as monotherapy due to the risk of resistance development and suboptimal pharmacokinetic properties in systemic infections. Current recommendations also note the role of sulbactam-containing regimens as therapy of choice for *A. baumannii*.

Infections caused by *A. baumannii* cause a wide spectrum of severe clinical conditions in critically ill patients. The most common forms are VAP, which develops in patients on mechanical ventilation, usually 48–72 hours after intubation. The pathogenesis of VAP is associated with microaspiration of oropharyngeal contents contaminated with *A. baumannii*, which colonises the airways through the endotracheal tube [15].

Bloodstream infections (sepsis and septic shock) caused by *A. baumannii* are characterised by high

mortality due to the microorganism's ability to cause a massive systemic inflammatory response. Sources of bacteraemia are often infected central venous catheters, pneumonia with haematogenous dissemination, or intra-abdominal infections [15].

Soft tissue and surgical wound infections caused by *A. baumannii* occur in postoperative patients and persons with polytrauma. CAUTI develop as a result of prolonged catheterisation of the bladder. Less common are meningitis (usually postoperative or associated with external ventricular drains), endocarditis, and osteomyelitis [2, 15].

These infections lead to a significant increase in hospitalisation duration (on average by 10–15 days), increased treatment costs (an additional $10,000–$40,000 per case), and increased mortality, which can reach 30–50 % with adequate therapy and 60–70 % with inadequate or delayed antibiotic therapy [15].

Risk factors for *A. baumannii* infection include prior use of broad-spectrum antibiotics (especially carbapenems, third- and fourth-generation cephalosporins, fluoroquinolones), which creates selective pressure and promotes survival of resistant strains. Prolonged stay in ICU (over 7 days) increases the risk of colonisation and infection through constant contact with the contaminated hospital environment. Invasive procedures play a key role: mechanical ventilation (especially prolonged, over 5–7 days) disrupts natural protective mechanisms of the airways; central venous catheters provide direct access to the bloodstream; urinary catheters serve as gateways for uropathogens; surgical interventions violate anatomical barriers [2–3].

Additional risk factors include immunosuppression (congenital or acquired, including HIV/AIDS, oncohaematological diseases, organ transplantation), diabetes mellitus, chronic kidney disease, chronic obstructive pulmonary disease, polytrauma, large-area burns, neurosurgical interventions, and elderly age (over 65 years). Of particular significance is prior colonisation with *A. baumannii*, which can persist for weeks and months, creating a reservoir for subsequent infection [2–3, 15].

The COVID-19 pandemic significantly affected the epidemiology of nosocomial infections caused by *A. baumannii*. Pathophysiological mechanisms that contributed to the development of secondary bacterial infections in COVID-19 patients included: direct damage to the respiratory epithelium by the SARS-CoV-2 virus, which reduced local immunity and facilitated bacterial adhesion; systemic immunosuppression due to lymphopenia and functional T-cell deficiency; "cytokine storm" with subsequent immune exhaustion; widespread use of corticosteroids (dexamethasone, methylprednisolone) and other immunosuppressive drugs (tocilizumab, baricitinib) for treatment of severe COVID-19 [5–6].

Prolonged hospital stay (often 2–4 weeks or more for critically ill patients), use of invasive procedures (mechanical ventilation was used in 15–30 % of hospitalised COVID-19 patients), and suppression of immune response created ideal conditions for severe secondary infections. Additional factors included: empirical widespread use of antibiotics in many COVID-19 patients (despite the viral aetiology of the disease), creating selective pressure; overload of healthcare systems, complicating adherence to standard infection control protocols; shortage of personal protective equipment in the initial phase of the pandemic; physical and emotional exhaustion of medical staff [5–6].

Studies conducted in various countries showed a significant increase in the frequency of nosocomial infections caused by *A. baumannii* amongst COVID-19 patients in ICUs. Meta-analysis of 30 studies (2020–2021) revealed that the frequency of secondary bacterial infections in COVID-19 patients in ICUs was 14–28 %, with *A. baumannii* being one of the most common isolates alongside *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus* [5–6].

The predominance of VAP as the main clinical form of *Acinetobacter* infection in our cohort is consistent with world literature data and meta-analyses [2,15]. A high proportion of patients with sepsis further emphasises the invasive nature of the infectious process and the propensity of *A. baumannii* for haematogenous dissemination.

The observed overall mortality in our study is within the range of literature data reported for infections caused by MDR strains of *A. baumannii* with adequate therapy, but remains unacceptably high [15]. Particularly alarming is the detection of extensively drug-resistant and pandrug-resistant isolates in our study population.

Molecular genetic analysis demonstrated predominance of the bla_{OXA-23} gene, corresponding to the epidemiological situation in Eastern Europe [12]. Detection of metallo-β-lactamase genes is particularly concerning, as these resistance determinants are easily transferred horizontally and are associated with poorer clinical outcomes.

Analysis of treatment efficacy demonstrated a clear advantage of combination therapy over monotherapy, supporting current IDSA recommendations for the treatment of infections caused by multidrug-resistant Gram-negative bacteria [14]. The combination of colistin plus tigecycline proved most effective, which

may be explained by the synergistic effect of drugs with different mechanisms of action.

WHO [1], CDC [2], and ECDC [3] recommendations emphasise the need for implementation of comprehensive antimicrobial stewardship (AMS) programmes to combat antibiotic resistance [16].

Study limitations should be noted, particularly its retrospective nature and relatively small number of patients (n = 50). Additionally, not all isolates were examined for the presence of all possible resistance genes.

Specifically, in our study, the E-test (Epsilometer test) was not used for determination of minimum inhibitory concentrations of carbapenems. This decision was justified, as for *A. baumannii*, the E-test has significant methodological limitations and is not recommended by international organisations due to slow and uneven growth of *A. baumannii* on culture media, risk of false results, and non-compliance with reference microdilution methods. EUCAST and CLSI explicitly state that gradient methods should not be used for determining susceptibility of *Acinetobacter* spp. to certain antibiotics [7, 17]. This method is unreliable for *A. baumannii*, especially regarding colistin, and is therefore excluded according to EUCAST/CLSI. Instead, we used standardised disc diffusion and broth microdilution methods according to EUCAST recommendations [7], which are the "gold standard" for *A. baumannii*.

It should also be noted that the RevoDx Sepsis Pathogen Detection Kit we used does not include the mcr gene, which encodes plasmid-mediated colistin resistance. Considering that colistin remains one of the key drugs for treatment of infections caused by multidrug-resistant strains of *A. baumannii* [7], monitoring of the mcr gene is critical for epidemiological surveillance. Further studies should include screening for this gene, especially in cases of phenotypic resistance to colistin [13].

Despite these limitations, the obtained data provide valuable information about the clinical and epidemiological features and resistance profiles of *A. baumannii* in the region in the context of the COVID-19 pandemic, emphasising the urgent need to optimise antimicrobial therapy and infection control strategies.

CONCLUSIONS

1. *A. baumannii* is one of the most clinically significant pathogens of nosocomial infections in intensive care units with a high mortality rate (36 %).

2. A high level of resistance to carbapenems (62 %) and fluoroquinolones (75 %) was detected, corresponding to average European indicators (60–65 %), whilst resistance to fluoroquinolones is higher and characteristic of Ukraine.

3. Colistin retains the highest activity (over 90 % susceptible isolates), tigecycline demonstrates moderate efficacy (60–75 %) and is most effective as part of combination regimens. Results should be interpreted cautiously, as EUCAST/CLSI have not established clinical breakpoints for tigecycline against *A. baumannii*.

4. The presence of acquired resistance genes, particularly bla_{NDM} and bla_{VIM}, is associated with worse prognosis and higher patient mortality. In our sample, survival was 25 % for bla_{NDM} (3 out of 12 patients) and 17 % for bla_{VIM} (1 out of 6 patients).

5. Combination antibiotic therapy demonstrates significantly higher efficacy compared to monotherapy: the combination of colistin plus tigecycline provided 78 % survival, whilst carbapenem monotherapy – only 42 %, which is consistent with IDSA recommendations. Current recommendations also note the role of sulbactam-containing regimens as therapy of choice for *A. baumannii*.

6. For effective control of *Acinetobacter* infections, a comprehensive approach is necessary, including strengthening infection control, implementation of antimicrobial stewardship programmes according to WHO, CDC, and ECDC recommendations, optimisation of antibiotic therapy protocols, and further research on the development of new therapeutic strategies.

PROSPECTS FOR FUTURE RESEARCH

Future research prospects include: expanding the patient sample and conducting a multicentre prospective study to confirm the obtained results; implementing molecular typing of *A. baumannii* strains to identify epidemic clones and transmission pathways; investigating the efficacy of new antibacterial agents and combination therapy regimens; assessing the impact of antimicrobial stewardship programmes on resistance indicators; and conducting molecular screening for the *mcr* gene to monitor colistin resistance.

AUTHOR CONTRIBUTIONS

A.V. Bondarenko – conception and design of the study, data collection and analysis, manuscript writing, final approval of the version for publication.

K.V. Yurko – data collection and analysis, interpretation of results, critical revision of the manuscript for important intellectual content, final approval of the version for publication.

D.V. Katsapov – clinical data collection, statistical data analysis, critical revision of the manuscript, final approval of the version for publication.

O.V. Bondarenko – microbiological research, molecular genetic analysis, interpretation of results, critical revision of the manuscript, final approval of the version for publication.

All authors agree to take responsibility for all aspects of the work, ensuring appropriate investigation and resolution of issues related to the accuracy or integrity of any part of the work.

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CONFLICT OF INTEREST

The authors declare no financial or non-financial conflicts of interest that could have influenced the results or interpretation of the data in this study. None of the authors have financial relationships with organisations that might have an interest in the published content over the past three years. The authors have no other relationships or activities that could have influenced the submitted work.

ARTIFICIAL INTELLIGENCE DISCLOSURE

During the preparation of this manuscript, the authors used AI-based tools (ChatGPT) exclusively for improving language style, editing, and grammar checking. After using these tools, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication. AI was not used for data analysis, interpretation of results, or formulation of scientific conclusions.

ETHICAL CONSIDERATIONS

The study was approved by the Ethics and Bioethics Commission of Kharkiv National Medical University, protocol №5 from 06.05.2026, and informed consent was obtained from all patients where possible.

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