

# EPIDEMIOLOGICAL HAZARD OF ANTIBIOTIC-RESISTANT MICROORGANISMS CURRENT THREATS AND CONTROL STRATEGIES

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## Abstract

Antibiotic-resistant microorganisms constitute one of the gravest threats to contemporary global public health, responsible for 1.27 million attributable deaths annually. This article examines the epidemiological burden of antimicrobial resistance, resistance transmission mechanisms, the clinical significance of ESKAPE pathogens in nosocomial settings, and evidence-based infection control and antibiotic stewardship strategies applicable to Central Asian healthcare institutions.

**Keywords:** Antimicrobial resistance, ESKAPE pathogens, spongiofibrosis, extended-spectrum beta-lactamase, carbapenem resistance, New Delhi metallo-beta-lactamase, multidrug-resistant organisms, nosocomial infection, horizontal gene transfer, antibiotic stewardship, epidemiological surveillance.

## Introduction

The accelerating global dissemination of antibiotic-resistant microorganisms has transformed a once-manageable pharmacological challenge into a genuine civilizational threat. The phenomenon of antimicrobial resistance (AMR) - defined as the capacity of pathogenic microorganisms to survive and proliferate in the presence of antimicrobial agents at concentrations that would ordinarily eliminate or suppress them - arises through complex biological, ecological, and behavioral mechanisms that span the boundaries between human medicine, veterinary practice, agriculture, and environmental science. Historically viewed as an exclusively clinical problem, AMR is now recognized by the World Health Organization as among the ten leading global public health threats, carrying implications for surgical safety, neonatal survival, management of immunocompromised patients, and pandemic preparedness. Understanding the precise epidemiological dimensions of this crisis is the essential precondition for any rational institutional or systemic response.

## Literature review

The foundational global epidemiological estimate of AMR burden was provided by the Antimicrobial Resistance Collaborators in their 2022 Lancet analysis, which attributed 1.27 million deaths directly to bacterial AMR in 2019, with *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Streptococcus pneumoniae*, and *Pseudomonas aeruginosa* accounting for 929,000 of these deaths. Russian epidemiologists have documented that healthcare-associated infections caused by multidrug-resistant organisms substantially increase hospitalization length, healthcare costs, and patient mortality compared to drug-susceptible equivalents. Briko and colleagues described the mechanisms by which nosocomial hospital strains acquire and consolidate



antibiotic resistance, emphasizing that the spread of resistant clones within wards proceeds through both direct patient-to-patient contact and indirect environmental contamination. Suksomchit and others established that the ESKAPE pathogen group - comprising *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species - is responsible for the overwhelming majority of treatment-refractory nosocomial infections worldwide. Uzbek infection control literature identifies unregulated antibiotic dispensing without prescription, insufficient microbiological diagnostic capacity, and gaps in sanitary-epidemiological oversight as primary drivers of resistance escalation in regional healthcare settings.

### Methodology

This study was conducted at the Infectious Disease Department and Clinical Microbiological Laboratory of the Fergana Regional Multidisciplinary Medical Center over a 24-month surveillance period from January 2022 to January 2024. The study employed a prospective descriptive-analytical epidemiological design combined with retrospective chart review for historical comparison. Study Population and Specimen Collection. A total of 1,240 clinical microbiological specimens were collected from 874 hospitalized patients during the observation period. Specimens included blood cultures (n=218), urine cultures (n=387), tracheal aspirates and bronchoalveolar lavage (n=214), wound swabs (n=261), and cerebrospinal fluid (n=160). Patients were included if they presented with clinical signs of infection occurring 48 hours after hospital admission (defining healthcare-associated infection, HAI), or if they were admitted with community-acquired infections requiring microbiological workup. Pediatric patients under 1 year and patients with previously documented immunosuppressive therapy were excluded from primary resistance-rate calculations to reduce confounding.

Microbiological Methods. Bacterial identification was performed using the VITEK 2 Compact automated system (bioMérieux, France). Antibiotic susceptibility testing was conducted by disk diffusion (Kirby-Bauer method) and minimum inhibitory concentration (MIC) determination using the broth microdilution method according to EUCAST 2022 breakpoints. Isolates were screened for extended-spectrum beta-lactamase (ESBL) production using the double disk synergy test (DDST) with cefotaxime/clavulanate and ceftazidime/clavulanate disks. Carbapenemase production was confirmed by the Modified Carbapenem Inactivation Method (mCIM) combined with EDTA-mCIM (eCIM) to differentiate metallo-beta-lactamases (MBL) from serine carbapenemases. Methicillin-resistant *Staphylococcus aureus* (MRSA) was identified by cefoxitin disk screening and confirmed by PCR detection of the *mecA* gene in a subset of isolates.

The incidence of HAI was calculated as cases per 1,000 patient-bed-days. Resistance rates were expressed as the percentage of resistant isolates among all tested isolates of each species. Temporal trends were analyzed by comparing the first 12-month period (2022) with the second 12-month period (2023). Risk factors for acquisition of multidrug-resistant organisms (MDRO) were assessed by univariate and multivariate logistic regression, incorporating variables: age, duration of prior hospitalization, prior antibiotic exposure within the preceding 90 days, presence of invasive devices (urinary catheter, central venous catheter, mechanical ventilator), and ward of admission (ICU versus



general ward). All analyses were conducted using SPSS v.26; statistical significance was defined at  $p < 0.05$ .

## Results

**Incidence of Healthcare-Associated Infections.** Over the 24-month surveillance period, a total of 312 HAI episodes were recorded among 874 included patients, yielding an overall HAI incidence rate of 9.7 cases per 1,000 patient-bed-days. The highest HAI incidence was observed in the intensive care unit (ICU), at 31.4 cases per 1,000 patient-bed-days, compared to 6.2 per 1,000 in general medical wards and 4.8 per 1,000 in surgical wards. The most common HAI categories were urinary tract infections (35.6%,  $n=111$ ), healthcare-associated pneumonia including ventilator-associated pneumonia (28.8%,  $n=90$ ), surgical site infections (19.9%,  $n=62$ ), and bloodstream infections (15.7%,  $n=49$ ).

**Pathogen Distribution and Resistance Rates.** Among 1,240 specimens, 718 yielded clinically significant bacterial isolates (57.9% positivity rate). ESKAPE pathogens collectively accounted for 61.3% ( $n=440$ ) of all isolates. The dominant organisms were *Klebsiella pneumoniae* ( $n=142$ , 19.8%), *Acinetobacter baumannii* ( $n=118$ , 16.4%), *Pseudomonas aeruginosa* ( $n=87$ , 12.1%), *Staphylococcus aureus* ( $n=61$ , 8.5%), *Escherichia coli* ( $n=189$ , 26.3%, included given its epidemiological significance), and *Enterococcus faecium* ( $n=32$ , 4.5%). ESBL production was confirmed in 63.4% ( $n=90$ ) of *K. pneumoniae* isolates and 48.1% ( $n=91$ ) of *E. coli* isolates. Carbapenem resistance was detected in 34.5% ( $n=49$ ) of *K. pneumoniae* isolates, of which mCIM/eCIM confirmed MBL production (predominantly NDM-type) in 28 (57.1%) and KPC-type serine carbapenemase in 12 (24.5%). Among *A. baumannii* isolates, carbapenem resistance reached 78.8% ( $n=93$ ), with colistin remaining the only consistently effective agent (susceptibility: 89.2%). MRSA prevalence among *S. aureus* isolates was 37.7% ( $n=23$ ). Vancomycin-resistant *Enterococcus faecium* (VRE) constituted 21.9% ( $n=7$ ) of *E. faecium* isolates.

**Temporal Trend Analysis.** Comparing 2022 to 2023, carbapenem resistance in *K. pneumoniae* increased from 28.3% to 40.9% ( $\Delta=+12.6$  percentage points). ESBL rates in *E. coli* rose from 43.7% to 52.6% ( $\Delta=+8.9$  percentage points). The proportion of pan-drug-resistant *A. baumannii* (resistant to all tested classes including colistin) remained low but emerged: 2 isolates in 2022 versus 5 isolates in 2023.

**Risk Factor Analysis.** Multivariate logistic regression identified the following independent risk factors for MDRO acquisition: ICU admission (OR 4.82, 95%CI 2.91-7.98,  $p < 0.001$ ), mechanical ventilation 5 days (OR 3.47, 95%CI 1.89-6.38,  $p < 0.001$ ), prior antibiotic exposure within 90 days (OR 2.91, 95%CI 1.74-4.86,  $p < 0.001$ ), urinary catheterization 3 days (OR 2.14, 95%CI 1.22-3.74,  $p=0.008$ ), and age 65 years (OR 1.88, 95%CI 1.12-3.16,  $p=0.017$ ).

## Discussion

The epidemiological findings of this study are alarming in both their absolute magnitude and their directional trajectory. A HAI incidence of 9.7 per 1,000 patient-bed-days - with ICU rates exceeding 31 per 1,000 - places the observed institution at a level consistent with reports from tertiary medical centers in comparable lower-middle-income regional contexts, but well above the benchmark targets of 5 per 1,000 patient-bed-days endorsed by European infection control standards. This gap is not primarily a reflection of inadequate clinical practice at the individual provider level; it reflects structural deficiencies in infection prevention infrastructure: insufficient single-isolation room



capacity, inconsistent hand hygiene audit programs, suboptimal stewardship of invasive device protocols, and limited real-time microbiological feedback loops between the laboratory and clinical teams. The resistance rates observed - carbapenem resistance in *K. pneumoniae* at 34.5% overall and rising to 40.9% by 2023, MRSA at 37.7%, and carbapenem-resistant *A. baumannii* at 78.8% - are consistent with the global trend described in the 2024 Lancet forecast study, which projects that deaths attributable to AMR will reach 1.91 million annually by 2050, with south Asia and adjacent regions bearing a disproportionate share of this burden. The emergence of NDM-type metallo-beta-lactamases as the dominant carbapenemase mechanism in our series is epidemiologically significant: NDM enzymes are encoded on highly mobile plasmids capable of horizontal gene transfer across diverse bacterial genera, meaning that their containment cannot be achieved through targeting a single clonal lineage. This molecular epidemiological reality demands whole-genome sequencing-based surveillance as a complement to - and eventually a replacement for - phenotypic susceptibility testing alone for outbreak response. The identification of prior antibiotic exposure within 90 days as a major independent risk factor (OR 2.91) confirms the fundamental ecological principle underlying AMR: antibiotic use at the individual level is not a neutral act but an evolutionary selective pressure with population-level consequences. Every unnecessary prescription, every incomplete treatment course, and every instance of prescription without microbiological confirmation contributes measurably to the resistance pool within the institution and, through patient transfers and environmental discharge, beyond it. Antibiotic stewardship programs - comprising prospective audit and feedback, formulary restriction of carbapenems and last-resort agents, and mandatory microbiological culture prior to empirical therapy escalation - represent the most evidence-supported intervention available to arrest the observed resistance escalation trajectory within the timeframe of meaningful clinical impact. Antibiotic-resistant microorganisms pose an escalating and quantifiable epidemiological threat, documented in this study by carbapenem resistance rates of 34.5% in *Klebsiella pneumoniae* and 78.8% in *Acinetobacter baumannii*. Institutional infection prevention and antibiotic stewardship programs, supported by systematic microbiological surveillance and regulatory enforcement of prescription standards, represent the essential and urgent response.

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