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PREVALENCE AND CONTROL METHODS OF ANTIBIOTIC-RESISTANT BACTERIA IN THE ANDIJAN REGION

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ABSTRACT: Background: Antimicrobial resistance (AMR) is a significant global public health threat, leading to increased morbidity, mortality, and healthcare costs. Regional data is crucial for developing targeted intervention strategies. This study aimed to investigate the prevalence of antibiotic-resistant bacteria and assess existing control mechanisms in healthcare facilities within the Andijan region of Uzbekistan. Methods: A cross-sectional study was conducted from January 2024 to August 2025 across five major multi-disciplinary hospitals in the Andijan region. A total of 650 clinical isolates were collected from various samples, including blood, urine, respiratory secretions, and wound swabs. Bacterial identification was performed using standard microbiological techniques and MALDI-TOF MS. Antimicrobial susceptibility testing (AST) was carried out using the Kirby-Bauer disk diffusion method, following the Clinical and Laboratory Standards Institute (CLSI) guidelines. Data on infection control policies and antibiotic stewardship programs were collected through structured questionnaires and interviews with healthcare personnel. Results: The most frequently isolated bacteria were *Escherichia coli* (31%), *Staphylococcus aureus* (24%), *Klebsiella pneumoniae* (18%), and *Pseudomonas aeruginosa* (11%). High resistance rates were observed among Gram-negative isolates to commonly prescribed antibiotics. *E. coli* showed significant resistance to ampicillin (>75%) and ciprofloxacin (>60%). Over 40% of *K. pneumoniae* isolates were resistant to third-generation cephalosporins, and 15% demonstrated carbapenem resistance. Among *S. aureus* isolates, 35% were identified as Methicillin-resistant *Staphylococcus aureus* (MRSA). Analysis of control measures revealed that while basic infection prevention protocols were in place, adherence was inconsistent, and dedicated antimicrobial stewardship programs were largely absent. Conclusion: The prevalence of multidrug-resistant bacteria, particularly carbapenem-resistant Enterobacteriaceae and MRSA, is a serious concern in the Andijan region. The findings underscore an urgent need for strengthening AMR surveillance, implementing robust antimicrobial stewardship programs, and enhancing infection prevention and control practices in healthcare settings across the region to mitigate the spread of resistant pathogens.

Keywords: Antimicrobial resistance, Andijan, Uzbekistan, *E. coli*, MRSA, Carbapenem resistance, Infection control, Antimicrobial stewardship.

INTRODUCTION

Antimicrobial resistance (AMR) has emerged as one of the most pressing challenges to global public health in the 21st century. The World Health Organization (WHO) has declared AMR a top 10 global public health threat, jeopardizing the efficacy of modern medicine (WHO, 2021). The progressive loss of effective antibiotics against common bacterial pathogens leads to prolonged illnesses, increased mortality rates, and substantial economic burdens on healthcare systems and national economies (O'Neill, 2016). Infections caused by multidrug-resistant (MDR) bacteria, which are resistant to at least three different classes of antimicrobial agents, are often difficult and expensive to treat, sometimes leaving no viable therapeutic options.

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The drivers of AMR are multifaceted and complex, encompassing the overuse and misuse of antibiotics in human medicine, veterinary practices, and agriculture; inadequate access to clean water, sanitation, and hygiene (WASH); poor infection prevention and control (IPC) in healthcare facilities; and a lack of rapid, affordable diagnostic tools (Laxminarayan et al., 2013). The global nature of travel and trade facilitates the rapid spread of resistant microorganisms across borders, making AMR a shared global responsibility.

While global surveillance systems like the WHO's Global Antimicrobial Resistance and Use Surveillance System (GLASS) provide a broad overview of the AMR landscape, data from specific regions, particularly in Central Asia, remain limited (WHO, 2022). Uzbekistan, as the most populous country in Central Asia, faces unique challenges related to its healthcare infrastructure, antibiotic prescription practices, and public awareness. Previous studies in Uzbekistan have highlighted concerning trends, including high rates of self-medication with antibiotics and the emergence of resistant strains like Methicillin-resistant *Staphylococcus aureus* (MRSA) and extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae (Parpieva et al., 2019; Kadirova et al., 2021).

The Andijan region, located in the Fergana Valley, is one of the most densely populated areas in Uzbekistan. Its healthcare system serves a large population, creating an environment where the selective pressure for antibiotic resistance can be particularly intense. However, there is a significant lack of localized, systematic data on the prevalence of specific resistant pathogens and the effectiveness of current control strategies within this region. Understanding the local epidemiology of AMR is fundamental for tailoring effective interventions, such as formulating local antibiotic guidelines, strengthening IPC measures, and implementing targeted antimicrobial stewardship programs (ASPs).

This study, therefore, aims to address this critical knowledge gap by providing a comprehensive assessment of the prevalence and patterns of antibiotic resistance among key bacterial pathogens isolated from patients in major hospitals in the Andijan region. Furthermore, it seeks to evaluate the existing infrastructure and practices for AMR control to identify key areas for improvement. The primary objectives are to identify the most common bacterial pathogens causing infections in hospitalized patients in the Andijan region, to determine the antimicrobial susceptibility patterns of these isolates to a panel of clinically relevant antibiotics, to estimate the prevalence of critical MDR organisms such as MRSA and carbapenem-resistant Enterobacteriaceae (CRE), and to assess the current state of IPC and antimicrobial stewardship practices in the participating healthcare facilities. The findings of this research are intended to provide evidence-based recommendations for local health authorities, hospital administrators, and clinicians to strengthen the fight against AMR in the Andijan region and contribute to the national action plan on antimicrobial resistance.

METHODS

Study design and setting - A prospective, cross-sectional, laboratory-based surveillance study was conducted between January 2024 and August 2025. The study involved five major multi-disciplinary public hospitals in the Andijan region, including the Andijan Regional Multi-Disciplinary Medical Center, Andijan City Emergency Medical Aid Hospital, and three district-level central hospitals. These facilities were selected to represent a mix of urban and semi-rural patient populations and different levels of healthcare delivery. Ethical approval for the study was obtained from the Ethics Committee of the Andijan State Medical Institute (Protocol #2023-12/A-3), and informed consent was obtained from patients or their legal guardians for the collection of clinical samples and data.

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Sample collection and processing - Non-duplicate clinical isolates were collected from routine diagnostic samples submitted to the microbiology laboratories of the participating hospitals. A total of 650 consecutive, clinically significant isolates were included in the study. The samples originated from various infection sites, including bloodstream infections (blood cultures), urinary tract infections (urine), respiratory tract infections (sputum, bronchial aspirates), and surgical site/wound infections (pus swabs). An isolate was considered clinically significant based on the laboratory's standard operating procedures and the treating physician's judgment. Basic demographic and clinical data (age, sex, hospital ward, and suspected diagnosis) were collected for each patient using a standardized data collection form.

Bacterial identification and antimicrobial susceptibility testing (AST) - Initial bacterial identification was performed at the respective hospital laboratories using conventional methods, including Gram staining, colony morphology on selective and differential media (e.g., MacConkey agar, Blood agar), and a series of biochemical tests (e.g., API 20E/NE, bioMérieux). All isolates were then transported to a central reference laboratory for confirmation and further characterization.

At the reference laboratory, species-level identification was confirmed using Matrix-Assisted Laser Desorption/Ionization-Time of Flight Mass Spectrometry (MALDI-TOF MS) (Bruker Daltonik, Germany).

Antimicrobial susceptibility testing was performed using the Kirby-Bauer disk diffusion method on Mueller-Hinton agar (MHA) plates. The procedure and interpretation of results were strictly based on the prevailing guidelines from the Clinical and Laboratory Standards Institute (CLSI M100, 33rd Ed.). The antibiotic disks (Oxoid, UK) tested were selected based on CLSI recommendations and local prescribing patterns. The comprehensive panel included specific antibiotics for different bacterial groups. For Enterobacteriaceae, the panel consisted of ampicillin, amoxicillin-clavulanate, piperacillin-tazobactam, cefazolin, ceftriaxone, ceftazidime, cefepime, imipenem, meropenem, gentamicin, amikacin, ciprofloxacin, and trimethoprim-sulfamethoxazole. For *Pseudomonas aeruginosa*, tested antibiotics included piperacillin-tazobactam, ceftazidime, cefepime, imipenem, meropenem, gentamicin, amikacin, and ciprofloxacin. The panel for *Staphylococcus aureus* comprised penicillin, oxacillin (using a cefoxitin disk for MRSA detection), erythromycin, clindamycin, gentamicin, ciprofloxacin, trimethoprim-sulfamethoxazole, and vancomycin. Lastly, for Enterococci, the tested agents were ampicillin, high-level gentamicin, and vancomycin.

Quality control and detection of specific resistance mechanisms - Quality control was ensured by testing reference strains, including *E. coli* ATCC 25922, *S. aureus* ATCC 25923, and *P. aeruginosa* ATCC 27853, with each batch of AST. Phenotypic tests were used to screen for specific resistance mechanisms. Isolates of *E. coli* and *K. pneumoniae* showing reduced susceptibility to ceftriaxone or ceftazidime were tested for ESBL production using the combination disk test (ceftazidime vs. ceftazidime-clavulanic acid and cefotaxime vs. cefotaxime-clavulanic acid). Enterobacteriaceae isolates with reduced susceptibility to imipenem or meropenem were screened for carbapenemase production using the Modified Carbapenem Inactivation Method (mCIM). *S. aureus* isolates were identified as MRSA based on resistance to cefoxitin (zone diameter ≤ 21 mm).

Assessment of infection control and stewardship practices - A standardized survey tool, adapted from the WHO's Infection Prevention and Control Assessment Framework (IPCAF), was used to evaluate IPC practices. Key personnel, including hospital epidemiologists, infection control nurses, and department heads (n=30), were interviewed. The survey covered areas such as hand

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hygiene programs, environmental cleaning, sterilization/disinfection procedures, and AMR surveillance capacity. A separate questionnaire was administered to clinicians (n=100) and pharmacists (n=20) to assess the presence and functionality of antimicrobial stewardship programs. Questions focused on the availability of local antibiotic guidelines, formulary restrictions, requirements for pre-authorization of broad-spectrum antibiotics, and practices of audit and feedback.

Data analysis - Data were entered into a database using WHONET 5.6 software and analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics (frequencies, percentages) were used to summarize the distribution of bacterial isolates and their resistance patterns. The prevalence of MDR, defined as non-susceptibility to at least one agent in three or more antimicrobial categories, was calculated. Chi-square or Fisher's exact tests were used to compare resistance rates between different species or hospital wards where appropriate. A p-value of <0.05 was considered statistically significant.

RESULTS

Distribution of bacterial isolates - A total of 650 non-duplicate bacterial isolates were collected and analyzed during the study period. The majority of the isolates were recovered from urine samples (38%), followed by wound/pus swabs (27%), respiratory samples (21%), and blood cultures (14%). Gram-negative bacteria constituted 65% (n=422) of all isolates, while Gram-positive bacteria accounted for 35% (n=228).

The four most prevalent pathogens identified were *Escherichia coli* (31.1%, n=202), *Staphylococcus aureus* (24.0%, n=156), *Klebsiella pneumoniae* (18.2%, n=118), and *Pseudomonas aeruginosa* (11.4%, n=74). Other less frequently isolated organisms included *Acinetobacter baumannii*, *Enterococcus* spp., and *Proteus mirabilis*.

Antimicrobial resistance patterns of gram-negative bacteria - The antimicrobial resistance patterns of the major Gram-negative isolates revealed high levels of resistance to several commonly used antibiotic classes.

Escherichia coli - As shown in Table 1, *E. coli* isolates exhibited extremely high resistance to ampicillin (78.2%) and trimethoprim-sulfamethoxazole (65.8%). Resistance to the fluoroquinolone ciprofloxacin was also alarmingly high at 61.4%. Resistance to third-generation cephalosporins was significant, with 48.5% of isolates resistant to ceftriaxone. Carbapenem resistance remained relatively low, with 5.9% of isolates resistant to imipenem. Phenotypic testing confirmed that 45.1% of *E. coli* isolates were ESBL producers.

Klebsiella pneumoniae - *K. pneumoniae* demonstrated higher resistance rates than *E. coli* across most antibiotic classes. Notably, 43.2% of isolates were resistant to ceftriaxone. The prevalence of carbapenem resistance was a major concern, with 15.3% of *K. pneumoniae* isolates showing resistance to imipenem. All carbapenem-resistant isolates were confirmed as carbapenemase producers by the mCIM test. Resistance to amikacin (22.0%) was lower compared to gentamicin (45.8%).

Pseudomonas aeruginosa - This opportunistic pathogen showed significant intrinsic and acquired resistance. Over 30% of isolates were resistant to ceftazidime (32.4%) and ciprofloxacin (36.5%). Resistance to the anti-pseudomonal carbapenems, imipenem and meropenem, was 24.3% and 21.6%, respectively.

Antimicrobial resistance patterns of gram-positive bacteria - Among Gram-positive organisms, the resistance patterns of *Staphylococcus aureus* were of primary clinical importance.

Staphylococcus aureus - Out of 156 *S. aureus* isolates, 35.3% (n=55) were identified as MRSA based on cefoxitin disk diffusion testing. All MRSA isolates were resistant to penicillin and

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erythromycin. A high rate of co-resistance to ciprofloxacin (67.3%) and gentamicin (41.8%) was observed among MRSA isolates. Importantly, all *S. aureus* isolates, including MRSA, remained susceptible to vancomycin.

Prevalence of multidrug resistance (MDR) - The overall prevalence of MDR was high among the key pathogens. Among *K. pneumoniae* isolates, 68% were classified as MDR. The MDR rates for *P. aeruginosa* and *E. coli* were 55% and 52%, respectively. For *S. aureus*, 41% of all isolates (which includes all MRSA strains) were MDR.

Assessment of AMR control measures - The survey results on IPC and antimicrobial stewardship practices revealed significant gaps. Regarding Infection Prevention and Control (IPC), all five hospitals had a designated IPC committee and basic protocols; however, implementation was inconsistent. Hand hygiene compliance, based on direct observation, was estimated to be below 40%, and the availability of alcohol-based hand rub was intermittent in several wards. Surveillance for healthcare-associated infections (HAIs) was passive and lacked systematic data collection and analysis. In terms of Antimicrobial Stewardship (ASP), none of the surveyed hospitals had a formal, dedicated ASP team. While four out of five hospitals had local antibiotic prescribing guidelines, clinicians reported they were often outdated and not actively promoted. There were no formulary restrictions or requirements for pre-authorization for broad-spectrum antibiotics like carbapenems and vancomycin. The practice of "de-escalation" of therapy based on culture results was not routinely followed, and over 70% of surveyed clinicians stated that pressure from patients or their families influenced their decision to prescribe antibiotics.

DISCUSSION

This study provides the first comprehensive, multi-center overview of the prevalence and patterns of antibiotic resistance in the Andijan region of Uzbekistan. The findings reveal a concerning landscape characterized by a high burden of infections caused by multidrug-resistant bacteria, coupled with significant deficiencies in the implementation of effective control measures.

The predominance of Gram-negative pathogens like *E. coli* and *K. pneumoniae*, particularly in urinary tract and wound infections, aligns with findings from other studies in Central Asia and globally (CAESAR Network, 2019). The alarmingly high resistance rates of *E. coli* to ampicillin, trimethoprim-sulfamethoxazole, and ciprofloxacin render these oral antibiotics largely ineffective for empirical treatment of community- and hospital-acquired infections in this region. This likely reflects decades of overuse and easy availability of these agents, often without a prescription (Belkina et al., 2014).

Of particular concern is the high prevalence of ESBL-producing *E. coli* (45.1%) and *K. pneumoniae*. This high rate severely limits the utility of third-generation cephalosporins, which are workhorse antibiotics in many hospital settings. The emergence of carbapenem-resistant *K. pneumoniae* (15.3%) is a red flag, signaling the arrival of a critical public health threat in the region. Carbapenem-resistant Enterobacteriaceae (CRE) infections are associated with extremely high mortality rates and limited treatment options, often forcing clinicians to use last-resort, more toxic, and expensive drugs like colistin (Falagas et al., 2014). The prevalence found in our study is higher than that reported in many European countries but is consistent with rising rates in other parts of Asia, highlighting the urgent need for aggressive containment strategies (Logan & Weinstein, 2017).

The prevalence of MRSA (35.3%) among *S. aureus* isolates is also a significant finding. This is a major driver of complicated skin and soft tissue infections, pneumonia, and bloodstream infections. While this rate is moderate compared to some global hotspots, it still poses a

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substantial challenge for infection management and control within hospitals (Lee et al., 2018). The fact that all *S. aureus* isolates remained susceptible to vancomycin is reassuring, but this underscores the critical importance of preserving the efficacy of this last-resort antibiotic through robust stewardship.

The deficiencies identified in IPC and ASP are likely major contributors to the high AMR rates observed. The low hand hygiene compliance is a fundamental failure in preventing cross-transmission of pathogens within healthcare facilities. The absence of functional ASPs means that antibiotic use is largely unregulated, promoting a continuous selective pressure for resistance. The lack of formulary restrictions and pre-authorization for broad-spectrum agents facilitates their overuse, accelerating the emergence of resistance to drugs like carbapenems. These findings are consistent with the WHO's assessment of AMR action plans in the region, which often points to gaps between policy and implementation (WHO, 2022).

This study has several limitations. First, it was conducted in five major hospitals and may not be fully representative of smaller healthcare facilities or outpatient settings in the region. Second, the study relied on phenotypic methods for resistance detection, and molecular characterization of resistance genes (e.g., *bla*KPC, *bla*NDM, *mecA*) was not performed, which would have provided deeper insights into the epidemiology of resistant strains. Finally, data on antibiotic consumption were not collected, which would have allowed for a direct correlation between usage and resistance patterns.

CONCLUSION AND RECOMMENDATIONS

In conclusion, this study documents a high prevalence of multidrug-resistant bacteria, including ESBL-producing Enterobacteriaceae, carbapenem-resistant *K. pneumoniae*, and MRSA, in the Andijan region. These findings indicate a serious public health challenge that requires immediate and coordinated action. The existing infection control and antimicrobial stewardship infrastructure is insufficient to address the scale of the problem.

Based on our findings, we propose several key recommendations. First, it is crucial to strengthen AMR surveillance by establishing a continuous, laboratory-based system linked to the national network, using standardized methods and software to track trends in real-time and inform policies. Second, implementing hospital-based Antimicrobial Stewardship Programs (ASPs) is essential; each hospital must establish a multidisciplinary committee to develop local guidelines, implement formulary restrictions, require pre-authorization for last-resort antibiotics, and provide regular audit and feedback to prescribers. Third, Infection Prevention and Control (IPC) practices must be enhanced with strong institutional support, focusing on improving hand hygiene compliance, implementing active surveillance for HAIs, and establishing contact precautions for patients with MDR organisms. Finally, launching educational campaigns for both healthcare professionals on rational antibiotic use and for the public on the dangers of self-medication is necessary. Addressing the threat of AMR in the Andijan region requires a sustained, multi-pronged effort involving policymakers, hospital administrators, clinicians, and the public. The findings from this study should serve as a catalyst for implementing these critical interventions to preserve the effectiveness of antibiotics for future generations.

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