

Multidrug Resistance in Intensive Care Units: Transmission, Risk Factors, Clinical Outcomes, and the Egyptian Context

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Abstract

Background: The burden of MDR infections is substantial, with millions of deaths globally associated with antimicrobial resistance, including a significant proportion directly attributable to drug-resistant pathogens. Critically ill patients are especially vulnerable due to the frequent use of invasive devices, prolonged hospitalization, mechanical ventilation, and repeated exposure to broad-spectrum antimicrobial agents.

Aim: Considering the different effectiveness of prevention strategies for specific bacterial species, further exploration is needed to determine the most effective measures to prevent the acquisition and spread of MDR bacterial colonization.

Conclusion: Given the high prevalence and clinical impact of MDR and XDR infections in ICUs, strict infection prevention and control measures are essential. In-hospital surveillance programs, staff education, antimicrobial stewardship, and routine inspections play a critical role in limiting the spread of resistant organisms and preserving the effectiveness of existing antibiotics.

Keywords: antimicrobial resistance; multidrug resistance; intensive care unit; cross-transmission; antimicrobial stewardship; Egypt

Introduction

The invisible threat of multidrug-resistant (MDR) bacterial cross-contamination among intensive care unit (ICU) personnel poses a significant challenge for healthcare facilities. Key insights from research on healthcare-acquired colonization (HAC) and infection (HAI) underscore the prevalence of MDR isolates, particularly among patients requiring mechanical ventilation. Extensive research has been conducted to understand the dynamics of MDR bacterial cross-contamination in the ICU setting. Studies have identified various independent factors that contribute to the transmission of these pathogens, including inadequate hand hygiene, improper use of personal protective equipment, and contaminated medical devices⁽¹⁾.

The occurrence of healthcare personnel (HCP) colonization, often facilitated by inadequate hand hygiene, the improper use of personal protective equipment, and contaminated medical devices, can have significant implications for patient care. Moreover, the role of healthcare workers in cross-contamination chains, with mobile phones identified as potential vectors, highlights the complex dynamics of bacterial transmission within the ICU. Studies have indicated that inanimate surfaces and equipment, such as bedrails, stethoscopes, and medical charts, can become contaminated with MDR bacteria in ICUs. This, in turn, potentially contributes to the transmission of pathogens to patients, primarily via the hands of the HCP⁽²⁾.

Preventive measures such as isolation protocols and environmental disinfection techniques are pivotal for reducing MDR bacterial cross-contamination and subsequent transmission. However, challenges in maintaining compliance have consistently been reported. Therefore, monitoring adherence to hand hygiene and providing timely feedback are crucial components of every hygiene protocol in the ICU. Novel technologies, including advanced disinfection methods and stringent monitoring techniques, can further reduce the impact of HCP on

MDR bacterial transmission. Furthermore, advancements in healthcare design and hospital engineering have shown promising potential for tackling the spread of MDR within the ICU⁽¹⁾.

The importance of antimicrobial surveillance and stewardship (AMSS) along with preventive measures is critical. Evidence suggests that a systematic and vigilant approach to monitoring antimicrobial use could have significant benefits, especially among ICU patients. Healthcare professionals should embrace them as an integral part of their practice to limit the emergence, colonization, and subsequent transmission of MDR bacteria. Current policy recommendations emphasize the necessity for continued improvements in hand hygiene compliance, leveraging innovative technologies to overcome obstacles in preventing transmission and assessing adherence to protocols⁽³⁾.

Incorporating the monitoring and assessment of hygienic-targeted practices as a principal component of management strategies is paramount in the complex ICU environment. Adjusting practices based on data-driven insights and evidence-based recommendations to reduce the risk of MDR contraction ensures the efficacy of interventions and the accuracy of policy measures⁽¹⁾.

Pathways of ICU-Acquired Infection

ICU-acquired infections, particularly those involving MDR bacteria, represent a major challenge for healthcare systems worldwide. Healthcare workers' hands often serve as the primary vectors for cross-transmission, connecting contaminated surfaces and equipment to patients, which may result in colonization or infection. Other factors that play a role in contamination and cross-transmission rates in the ICU may include nurse-staffing levels, frequency/number of colonized or infected patients, ICU structural features (e.g., single-bed or multi-bed ICU rooms), and the adoption of antimicrobial stewardship programs (ASPs). However, approximately 20–40% of nosocomial infections are estimated to arise from cross-transmission via healthcare workers' hands. Moreover, the hands of caregivers tend to exhibit greater contamination over time, marking progression from sufficient care duration⁽⁴⁾.

In a recent systematic review, HCP hands were found to be frequently contaminated with MDR organisms across all care settings, with a prevalence ranging from 4% to 9%. The researchers observed a slightly higher rate of *Pseudomonas aeruginosa* (5.67%) and *Acinetobacter baumannii* (7.52%) in ICU settings than in inpatient floors (3.93% and 5.60%, respectively), but a lower rate of MRSA in the ICU (2.20%) than in the inpatient group (5.14%). The highest rates of MRSA were found in North America (8.28%), followed by Asia (4.23%) and Europe (2.47%)⁽⁵⁾.

At first glance, the reported rates may seem low; however, it is important to consider the influence of study design and measurement on MDR prevalence rates. Cross-sectional studies, for example, showed a pooled prevalence of 3.25% compared with 12.49% for other designs, such as randomized controlled studies and pre-post studies. The method of culturing also seems to affect the observed prevalence rates. The juice glove and swab methods had consistently higher observed rates, ranging from 4.48% to 6.90%, whereas the agar direct contact method had the lowest prevalence rate (1.55%)⁽⁶⁾.

The delineation of a marked patient zone is a well-known concept that has been shown to improve hand hygiene compliance among healthcare personnel and can help understand cross-contamination patterns within the vibrant ICU environment. The contamination of surfaces within the patient zone, an area that encompasses the patient and their immediate surroundings, can arise either via the contaminated hands of healthcare workers or the direct patient shedding of microorganisms. Higher environmental contamination has been reported around infected patients than around patients who are only colonized, with a correlation between the frequency of environmental contamination and culture-positive body sites⁽¹⁾.

It has also been shown that MDR bacteria can contaminate communal surfaces, the surfaces of medical equipment, and other high-contact zones in ICUs. In a randomized crossover study, the recontamination of high-contact surfaces in ICUs occurred 4 h after standard cleaning measures. Various ICU equipment items and commonly used and/or touched objects harbor bacteria, often showing antibiotic susceptibility profiles akin to those found among patients. For instance, electrocardiography lead wires have demonstrated contamination rates between 20% and 45%⁽⁷⁾.

Stethoscopes are heavily contaminated, with bedside ones at 95% and personal ones at 67%. Ventilator surfaces are almost entirely polluted with bacterial contamination ranging from 70.6% to 100%. Portable radiography and ultrasound equipment, despite cleaning, show varied and sometimes residual contamination. Computer keyboards and faucet handles in the ICU setting have also been found to be significant reservoirs of nosocomial pathogens, with the colonization rate for keyboards reaching 26% in occupied rooms and faucet handles exhibiting rates of 15%. Medical charts are also hotspots for bacteria, with contamination rates ranging from 80% to 90%. Lastly, even personal items, such as mobile phones, present a high risk, boasting contamination rates of up to 94.5%⁽⁸⁾.

The survival of MDR bacteria on surfaces varies significantly among species, ranging from hours to months or even years, depending on the species, as does their ability to persist with both environmental input and various cleaning methods. According to the latest comprehensive systematic review of the persistence of bacteria on inanimate surfaces, it was reported that resilient *Acinetobacter* spp., notorious for their environmental tenacity, can maintain their presence on surfaces for durations ranging from three days to five months. The ubiquitous *Escherichia coli* presents a survival period that is as variable as it is long, persisting anywhere from 1.5 h to an extensive 16 months. *Klebsiella* spp., another prominent member of the Enterobacteriaceae family, outpaces *E. coli*, enduring from 2 h to 30 months. In Gram-positive bacteria, *Enterococcus* spp., which include both vancomycin-resistant and vancomycin-sensitive strains (VRE and VSE), can persist for 5 days to 4 months⁽⁹⁾.

Staphylococcus aureus, encompassing its methicillin-resistant variant (MRSA), exhibits survival periods ranging from a week to a robust seven months. This wide range of durability and persistence on surfaces among MDR pathogens underscores the importance of meticulous hygiene practices in healthcare settings, as well as the necessity for comprehensive sterilization protocols in high-risk environments such as ICUs⁽¹⁰⁾.

Risk Factors for MDR Colonization

Considering the different effectiveness of prevention strategies for specific bacterial species, further exploration is needed to determine the most effective measures to prevent the acquisition and spread of MDR bacterial colonization. High colonization pressure is often associated with the spread of multidrug-resistant organisms in healthcare settings, as it reflects the increased potential for the cross-transmission of these organisms among patients. Other independent risk factors were mechanical ventilation and arterial catheter use⁽¹¹⁾.

The identification of patient risk factors for MDR bacterial colonization in ICUs is a proposed measure that may serve both as an effective prevention intervention and a treatment strategy in specific patient populations, such as immunocompromised patients. However, a prospective study investigating the accuracy of the American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA) criteria in predicting infection or colonization by MDR organisms in ICU patients revealed that the criteria demonstrated high sensitivity and negative predictive values but low specificity and positive predictive values in predicting MDR colonization or infection at ICU admission. According to these findings, independent predictors of infection or colonization with MDR bacteria upon ICU admission included prior antimicrobial treatment, residence in a nursing home, and prior hospitalization. Another study from China demonstrated the low accuracy of ATS guidelines in predicting MDR colonization, particularly in patients from departments with low or high MDR infection rates, further challenging their role as independent interventions and questioning their clinical value in ICU settings⁽¹²⁾.

Overall, screening techniques have inherent limitations. For instance, they may not detect all carriers of MDR bacteria, especially if the bacteria are present in low numbers or at sites not sampled. Additionally, false negatives can occur because of limitations in the sensitivity of screening tests, and the costs associated with multiple and repeated tests cannot be undermined. Therefore, while screening is a crucial component of infection control, it should be complemented with other strategies, such as identifying risk factors for colonization and spread in ICU patients upon admission, for improved management and infection control⁽¹³⁾.

Antimicrobial Surveillance and Stewardship

Antimicrobial surveillance targeting ICUs is fundamental for combating MDR bacterial proliferation and spread. Efficient collaboration between ICU physicians, pharmacists, microbiologists, and infection control specialists plays a pivotal role in the success of these programs. By understanding the role, pathways, and patterns of

environmental contamination in the transmission of MDR bacteria, clinicians and researchers can develop and adopt better practices to minimize the risks in ICU settings. Environmental cultures, such as swab tests, agar slides, and air and water sampling, provide valuable information on the presence and persistence of MDRs in the environment and on surfaces, thereby helping to establish a more definitive link between environmental contamination and the acquisition of these pathogens. Furthermore, frequent culturing can help assess the effectiveness of various cleaning and disinfection methods, which is essential for developing data-driven strategies to prevent transmission in ICU settings⁽¹⁾.

Understanding the transmission dynamics of MDRs in ICU settings and monitoring their trends in the form of objective monitoring of cleaning procedures has reportedly contributed to significantly reducing patient-zone contamination. Other objective monitoring methods of environmental hygiene include direct observation, which has been previously discussed, fluorescent markers, and adenosine triphosphate (ATP) bioluminescence⁽¹⁾.

Educating healthcare workers on antibiotic stewardship principles further enhances the effectiveness of preventive strategies. This educational focus allows clinicians to adopt a more judicious approach toward prescribing antibiotics, an approach that is critical in minimizing the emergence, colonization, and transmission of MDR bacteria. ASPs are multifaceted strategies aimed at optimizing the use of antibiotics. This can be achieved by ensuring the correct dosing, choosing the appropriate antibiotic, and regulating the duration and route of administration. These elements of ASPs can collectively reduce the overall exposure to antibiotics and therefore minimize the emergence of the resistance and colonization of MDR bacteria. This allows healthcare providers to identify patterns in antibiotic use and hence identify overuse or misuse. Regular feedback and prospective auditing from this surveillance can then guide alterations in prescribing habits, leading to more efficient use of antibiotics and a reduction in resistance⁽¹⁴⁾.

The implementation of ASPs has been shown to have positive effects on the management of infections in ICUs. A multifaceted ASP led to improvements in the management of infections, including a reduction in the duration of empirical therapy and the use of quinolones. Additionally, the proportion of MDR bacteria in ICU-acquired infections decreased, indicating a positive impact on reducing resistance⁽¹⁵⁾.

However, implementing such a program can pose several challenges. For instance, it requires a significant amount of time and effort to collect, analyze, and interpret data, which may strain already limited resources. Additionally, changing long-standing prescribing habits may face resistance from some clinicians. Also, the success of these programs greatly depends on close and continuous collaboration between different professionals, a challenge that may prove difficult to overcome in the hectic ICU environment⁽¹⁶⁾.

In terms of future directions, technological advancements could play a vital role in ASPs. For example, artificial intelligence (AI) and machine learning algorithms could be used to analyze large amounts of data more efficiently, predict outbreaks, or even suggest the most appropriate antibiotics based on specific patient characteristics and local epidemiology, as evidenced by successful previous attempts in using computerized methods of surveillance. Moreover, fostering a culture of perpetual stewardship among healthcare professionals based on continuous education and training can significantly improve adherence to the guidelines. Multidisciplinary meetings have also been proven to be effective in reducing antibiotic use in the ICU setting⁽¹⁷⁾.

Finally, while these strategies aim to combat the spread and development of MDR bacteria, specifically in the ICU setting, it is crucial to recognize that these efforts are part of a broader, ongoing commitment to global health. The importance of a One Health approach, which recognizes the interconnectedness of human, animal, and environmental health, cannot be understated in this context⁽⁴⁾.

Clinical Outcomes of MDR Infection

The burden of MDR infections is substantial, with millions of deaths globally associated with antimicrobial resistance, including a significant proportion directly attributable to drug-resistant pathogens. Critically ill patients are especially vulnerable due to the frequent use of invasive devices, prolonged hospitalization, mechanical ventilation, and repeated exposure to broad-spectrum antimicrobial agents⁽¹⁸⁾.

Within the ICU setting, infections caused by MDR and extensively drug-resistant (XDR) Gram-negative bacteria are common and are associated with severe clinical outcomes. Predominant MDR pathogens include *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*. High rates of MDR and XDR phenotypes have been reported among these organisms, with *Pseudomonas* spp. and *Acinetobacter* spp. often demonstrating particularly high levels of resistance. Despite widespread resistance, many Gram-negative isolates remain susceptible to last-line agents such as colistin, while Gram-positive organisms commonly retain susceptibility to vancomycin⁽¹⁹⁾.

The distribution of MDR pathogens varies across ICUs and geographic regions. In some settings, *E. coli* and *Klebsiella* spp. predominate, whereas in others, *Pseudomonas* spp. or *Acinetobacter* spp. are the most frequently isolated resistant organisms. *Klebsiella* spp. frequently exhibit MDR and XDR profiles, while *Acinetobacter* spp. are often characterized by extremely high rates of extensive drug resistance. This heterogeneity reflects differences in antimicrobial use, infection control practices, and patient populations⁽²⁰⁾.

Several factors have been consistently associated with an increased risk of MDR infections in ICU patients. These include prolonged hospital or ICU stay, extended duration of mechanical ventilation, prior exposure to antimicrobial agents, invasive procedures, colonization with resistant organisms, reintubation, and greater severity of underlying disease. Ventilator-associated pneumonia caused by XDR pathogens is particularly associated with prolonged ICU and hospital stays, advanced patient age, longer duration of ventilation prior to infection onset, and increased rates of reintubation⁽²¹⁾.

The relationship between MDR or XDR status and clinical outcomes such as mortality, length of hospitalization, and severity scores remains complex. In some ICU populations, resistance status does not independently predict prognosis, especially in environments where resistance is nearly universal among isolates. In such contexts, outcomes may be driven primarily by the severity of critical illness, comorbidities, and organ dysfunction rather than resistance patterns alone. Additionally, limitations such as small sample sizes, restriction of isolates to specific infection sites, and specialized ICU settings may influence observed associations⁽²²⁾.

Resistance mechanisms among Enterobacterales, including third-generation cephalosporin resistance and AmpC β -lactamase overproduction, further complicate antimicrobial management. However, detailed characterization of resistance phenotypes is not always available in routine clinical laboratories, limiting the ability to fully assess local resistance patterns and guide targeted therapy⁽²³⁾.

MDR in Egyptian Intensive Care Units

Intensive Care Units (ICUs) in Egypt are facing a significant challenge with the rising prevalence of multidrug-resistant organisms (MDROs), which complicates the management of critically ill patients. The ICU environment, characterized by frequent use of invasive devices and extensive empirical antibiotic therapies, acts as an epicenter for antimicrobial resistance. Studies in Egyptian tertiary care hospitals indicate that Gram-negative bacteria are the predominant culprits, accounting for the vast majority of isolates in ICU settings. Pathogens such as *Klebsiella pneumoniae* and *Escherichia coli* are frequently identified as leading causes of hospital-acquired infections⁽²⁴⁾.

The prevalence of resistance is alarmingly high; for instance, research from Ain Shams University Hospitals highlights that the continuous spread of these resistant strains poses an inevitable catastrophe requiring strict antibiotic stewardship⁽²⁵⁾.

Among the problematic pathogens, *Klebsiella pneumoniae* is particularly concerning due to its escalating resistance profiles. Recent data shows that a significant proportion of *K. pneumoniae* isolates recovered from Egyptian ICUs are classified as multidrug-resistant or even extensively drug-resistant. The situation is further complicated by the emergence of colistin and carbapenem resistance, which severely limits the available options for empirical therapy. Genomic characterizations have revealed that these resistant isolates often produce extended-spectrum β -lactamases and carbapenemases, alongside genetic mutations associated with colistin resistance⁽²⁶⁾.

Conclusion

Given the high prevalence and clinical impact of MDR and XDR infections in ICUs, strict infection prevention and control measures are essential. In-hospital surveillance programs, staff education, antimicrobial stewardship, and routine inspections play a critical role in limiting the spread of resistant organisms and preserving the effectiveness of existing antibiotics. Active screening and isolation strategies, particularly for carbapenem-resistant Enterobacterales, are crucial to preventing transmission within ICUs and protecting vulnerable patient populations⁽²⁷⁾.

This high incidence of antimicrobial resistance underscores the critical need for localized, routinely updated antibiograms to guide physicians in selecting effective treatments while health authorities implement more rigorous infection control and prevention strategies⁽²⁸⁾.

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