REVIEW ARTICLES

Tackling Infections in Intensive care unit setting

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ABSTRACT

Infections within the intensive care unit (ICU) continue to be a major contributor to morbidity and mortality throughout Europe. Critically ill patients, oftentimes presenting with organ failure, having frequent interactions with invasive medical devices, and by receiving multiple antimicrobial agents are particularly susceptible to infections. Having knowledge of pathogen-specific epidemiology in ICUs across Europe and their antimicrobial resistance patterns is of utmost importance to choosing the right empirical therapy. Challenge posed by multidrug-resistant organisms, especially Gram-negative bacteria, is easier to tackle with infection prevention strategies, antimicrobial stewardship initiatives, and collaborative multidisciplinary care in place within the ICU setting.

Keywords: ICU; infections; MDRO

Introduction

Healthcare-associated infections (HAIs) represent one of the most significant challenges in intensive care medicine. Intensive care unit (ICU) patients experience infection rates that are several times higher than patients in general hospital wards (1). It is mostly due to the immune dysfunction and high prevalence of invasive procedures done on patients in ICU. Infections are associated with prolonged ICU stay, increased healthcare costs, and excess mortality, particularly when caused by multidrug-resistant organisms (MDROs)(2).

The EPIC III study, involving ICUs across Europe and beyond, reported that 54% of ICU patients had suspected or confirmed infection, with 22% acquiring infection after ICU admission. That highlights the disease burden of ICUs, as more than half of the patients will be treated for an infection, and almost half of those patients will contract an infection in the ICU. Pneumonia accounts for most of the ICU infections, followed by bloodstream and urinary tract infections (3). European Centre for Disease Prevention and Control (ECDC) surveillance reports consistently identify ICUs as the hospital setting with the highest prevalence of HAIs. Approximately 15–25% of ICU patients develop at least one HAI during their stay, with considerable differences among countries. Mechanical ventilation, central venous catheterization, and urinary catheterization are strongly associated with increased risk of infection. More than 60% of ICU-acquired pneumonias are ventilator-associated, approximately one-third of bloodstream infections (BSIs) are central line-associated, and nearly all ICU-acquired urinary tract infections (UTI) occur in catheterized patients in Europe (Table 1.). Apart from bacterial infections, fungal and viral pathogens are increasingly recognized as contributing agents to an infectious burden in ICUs (4).

Widespread dissemination of bacterial strains harboring multiple resistance genes to antimicrobial agents has further complicated the management of ICU infections, with regards to empirical therapy and contact precautions regarding patients colonized or infected with those strains. Surveillance data from the European

Antimicrobial Resistance Surveillance Network (EARS-Net) outlines persistently high resistance rates among Gram-negative microorganisms, particularly *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and carbapenem-resistant Enterobacterales (5). These trends have important implications for induction of antimicrobial therapy, infection control measures and finally on clinical outcome in critically ill patients.

Table 1. Estimated prevalence of infectious syndromes in European ICUs.

Infectious syndrome	Estimated proportion of ICU HAIs (%)	Risk factor	References
Ventilator-associated pneumonia	40–50	Mechanical ventilation	Vincent et al. (2020); ECDC (2021); Koulenti et al. (2017)
Bloodstream infection	7–10	Central venous catheter	Munro et al. (2024); Tabah et al. (2012); ECDC (2021)
Catheter-associated urinary tract infection	3–5	Urinary catheter	ECDC (2021); Hooton et al. (2010)
Intra-abdominal infection	5–8	Surgical procedures, drains	Munro et al. (2024); Tabah et al. (2012)
Fungal infections (mainly candidemia)	5–10 (of BSIs)	Central venous catheter	Munro et al. (2024); Vincent et al. (2020); Pappas et al. (2016)

Ventilator-associated pneumonia in the ICU

Ventilator-associated pneumonia (VAP) remains the most frequently reported ICU-acquired infection in Europe. Although prevention strategies have reduced incidence in some settings, VAP continues to account for up to half of ICU HAIs (6,7). ICU patients oftentimes require prolonged mechanical ventilation and frequently exposed to multiple antimicrobial agents, both of which contribute to infections with difficult-to-treat microorganisms.

Gram-negative bacteria are the predominant cause of VAP in Europe (Table 3.). *Pseudomonas aeruginosa* is the most frequently isolated pathogen, followed by *Staphylococcus aureus*, *Klebsiella* spp., *Escherichia coli*, *Enterobacter* spp., and *Acinetobacter baumannii* (7,8). Antimicrobial resistance is common among VAP pathogens. Carbapenem resistance in *P. aeruginosa* and *A. baumannii* and ESBL production among Enterobacterales complicates empirical antimicrobial therapy, while being associated with increased ICU patient mortality (5). Further implications of difficulties when prescribing empirical therapy are carbapenem resistance among *P. aeruginosa* and *A. baumannii* isolates, with carbapenems being the agent of choice for ESBL producing Enterobacterales.

Table 2. Pathogens associated with VAP in European ICUs.

Pathogen	Estimated frequency among VAP isolates (%)	Resistance	References
Pseudomonas aeruginosa	20–30	carbapenem resistance	Koulenti et al. (2017)
Staphylococcus aureus	15–20	methicillin resistance	Vincent et al. (2020)
Klebsiella spp.	15–20	beta-lactam resistance	ECDC (2021)
Escherichia coli	10–15	beta-lactam resistance	Koulenti et al. (2017)
Enterobacter spp.	5–10	beta-lactam resistance	Koulenti et al. (2017)
Acinetobacter baumannii	5–10	extensive drug resistance	ECDC (2021)

Bloodstream infections in the ICU

Bloodstream infections represent one of the most severe ICU-acquired infections and are consistently associated with high mortality. Population-based and ICU-specific studies report mortality rates ranging from 30% to over 40%, depending on pathogen, resistance profile, and patient comorbidities (2,9).

It is estimated that ICU-acquired BSI incidence falls in the 1.5–3 episodes per 1,000 patient-days in Europe (10). The EUROBACT study demonstrated that the majority of ICU BSIs are secondary, most frequently originating from pneumonia, intra-abdominal infections, or urinary tract infections (11). Primary catheter-related BSIs remain common but can be curbed by active prevention programs (12).

Both Gram-positive and Gram-negative microorganisms cause BSIs in ICUs across Europe (Table 2.). Coagulase-negative staphylococci, *Enterococcus* spp., and *Staphylococcus aureus* are among most common Gram-positive isolates, while *Klebsiella* spp., *Escherichia coli*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii* are the most common Gram-negative isolates (2,3). Fungal pathogens, predominantly *Candida* spp., account for 5–10% of ICU BSIs and are associated with worse outcomes, especially when diagnosis or antifungal therapy is delayed (13).

Table 3. Bacterial and fungal pathogens causing ICU BSIs in Europe.

Pathogen	Approximate proportion of ICU BSIs (%)	Resistance	References
Coagulase-negative staphylococci	20–30	methicillin resistance	Munro et al. (2024); Tabah et al. (2012); Vincent et al. (2020)
Enterococcus spp.	10–15	vancomycin resistance	Lanaghan et al. (2024); ECDC (2021)
Staphylococcus aureus	10–15	methicillin resistance	Vincent et al. (2020)
Klebsiella spp.	8–12	beta-lactam resistance	Munro et al. (2024); ECDC (2021)
Escherichia coli	7–10	beta-lactam resistance	Munro et al. (2024)
Pseudomonas aeruginosa	5–10	carbapenem resistance	ECDC (2021)
Candida spp.	5–10	azole resistance	Munro et al. (2024); Pappas et al. (2016)
Acinetobacter baumannii	2–5	extensive drug resistance	Munro et al. (2024); ECDC (2021)

Other infection types in the ICU

Intra-abdominal infections represent a very high portion of ICU infections, with some estimates ranging from 5-20% of all ICU patients having one (14,15). Gram-negative bacteria are among the most isolated pathogens involved in intra-abdominal infections, with *E. coli* being the predominant pathogen isolated (16). *Enterococcus* spp. was the most common gram-positive isolate responsible for intra-abdominal infections in ICU. Mortality of patients with intra-abdominal infections is usually higher than of those associated with other infections (15).

ICU-acquired UTIs represent a smaller proportion of HAIs and are almost universally catheter-associated. Risk for contracting an infection increases with catheter duration and prior antimicrobial exposure (17). Common pathogens are *E. coli*, *Enterococcus* spp., *Klebsiella* spp., *P. aeruginosa*, and *Candida* spp. While mortality directly attributable to catheter associated UTI is lower than for BSI or VAP, these infections contribute to overuse of antimicrobial agents, consequential resistance selection in pathogens, and prolonged ICU stay of patients.

Fungal infections, particularly invasive candidiasis, have seen an increase in incidence in European ICUs. Risk factors for contracting an invasive fungal infection include usage of broad-spectrum antibiotics, presence of central venous catheters, parenteral nutrition, and immunosuppression of patients (13). Candidemia is associated with high mortality and prolonged hospitalization, emphasizing the importance of early diagnosis of invasive fungal infections, with subsequent appropriate and timely antifungal therapy induction.

Respiratory viruses are recognized as an important cause of ICU admission, which can further contribute to secondary bacterial infections in ICU patients. Influenza, SARS-CoV-2, and other respiratory viruses can cause severe pneumonia requiring mechanical ventilation (18,19). As stated, viral infection may predispose patients to secondary bacterial infection and complicate antimicrobial stewardship decisions (20). COVID-19 pandemic highlighted the vulnerability of ICU patients to secondary BSIs, with a severe impact on infection prevention programs due to system and personnel strain in healthcare systems across the world (21,22).

Antimicrobial resistance and prevention strategies in the ICU

Antimicrobial resistance remains a challenge in treating ICU infections, with understanding the local epidemiology and resistance patterns being of utmost importance in choosing the appropriate empirical therapy (Table 4.). MRSA remains prevalent in European ICUs, accounting for 15–25% of *S. aureus* isolates (3). Vancomycin-resistant *Enterococcus* is less common but increasing in some European regions (6). Gram-negative resistance poses the greatest threat to ICU infection management. EARS-Net data demonstrate high rates of carbapenem resistance in *A. baumannii* (60–85%), substantial resistance in *P. aeruginosa* (20–30%), and increasing carbapenemase production among Enterobacterales (5). Resistance patterns vary from country to country, underlying the need for knowledge of local epidemiology. Infections caused by resistant organisms are independently associated with increased mortality, delayed appropriate therapy, and excess healthcare costs (2).

Effective prevention strategies for reducing the impact of resistance include proper management of central line catheters, mechanical ventilation, doing proper hand hygiene in ICUs and appropriate environmental cleaning (12,23). Antimicrobial stewardship programs play a critical role in optimizing therapy, reducing unnecessary antibiotic exposure and limiting resistance to antimicrobials (10,24).

ICU-acquired infections remain a major burden across Europe, driven by specific high-risk pathogens and increasing antimicrobial resistance. Bloodstream infections, intra-abdominal infections and ventilator-associated pneumonia are the most dominant clinical entities comprising the landscape of ICU-acquired infections, with Gram-negative MDROs posing the greatest challenge regarding treatment choice. Sustained surveillance, prevention, and multidisciplinary management are essential to improve outcomes of these infections in critically ill patients. Further studies assessing the local and global epidemiological data are needed to guide empirical treatment and implementation of rapid microbiological testing could benefit individualised and targeted therapy for patients in the ICU setting.

Table 4. Antimicrobial resistance rates among ICU pathogens in Europe.

Pathogen	Resistance	Approximate prevalence (%)	References
Staphylococcus aureus	methicillin resistance	15–25	Vincent et al. (2020)
Enterococcus spp.	vancomycin resistance	5–15	ECDC (2021)
Pseudomonas aeruginosa	carbapenem resistance	20–30	ECDC (2021)
Klebsiella spp.	ESBL production	20–40	Munro et al. (2024); ECDC (2021)
Klebsiella spp.	carbapenem resistance	8–15	Munro et al. (2024); ECDC (2021)
Acinetobacter baumannii	carbapenem resistance	60–85	Munro et al. (2024); ECDC (2021)

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