



Review article

Comprehensive hygiene strategies against healthcare-associated infections caused by *Clostridioides difficile*

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Sofía Geraldine Avilés Figueroa^{1*}, Nadia Patricia Rodríguez Villalta²

1,2. National Institute of Health, Ministry of Health, San Salvador, El Salvador.

*Correspondence

✉ sgavilesf92@gmail.com

1. 0009-0002-5330-7068

2. 0000-0002-2725-9210

Abstract

Clostridioides difficile is a spore-forming Gram-positive bacterium. *Clostridioides difficile* infection ranges from mild diarrhea to fatal pseudomembranous colitis. It is currently the most prevalent and costly healthcare-associated infection, contributing to 17 % of deaths. Infection in hospitals is diagnosed after three days of hospitalization. Globally, *Clostridioides difficile* infection is a serious problem that affects patient safety and the quality of healthcare. A narrative review was conducted to synthesize the available evidence on healthcare-associated *Clostridioides difficile* infections and the comprehensive hygiene strategies described for their prevention and control. The search was conducted in the Medline, Lilacs, and SciELO databases. Original articles and narrative reviews published between 2020 and 2025 in English and Spanish were included. Studies showed that hand hygiene and rigorous environmental cleaning are essential to reduce the transmission of *Clostridioides difficile*. Effective management requires a comprehensive approach that includes the use of sporicides, appropriate administration of antimicrobials, and training of healthcare personnel.

Keywords

Clostridioides difficile, Hand Hygiene, Cross Infection, Epidemiology.

Resumen

Clostridioides difficile es una bacteria grampositiva formadora de esporas. La infección por *Clostridioides difficile* varía desde una diarrea leve hasta una colitis pseudomembranosa mortal. Actualmente, es la infección asociada a la atención sanitaria más prevalente y costosa, que contribuye al 17 % de las muertes. La infección en hospitales se diagnostica después de tres días de hospitalización. A nivel mundial, la infección por *Clostridioides difficile* es un problema grave, que afecta la seguridad del paciente y la calidad de la atención sanitaria. Se llevó a cabo una revisión narrativa con el objetivo de sintetizar la evidencia disponible sobre las infecciones asociadas a la atención en salud por *Clostridioides difficile* y las estrategias de higiene integral descritas para su prevención y control. La búsqueda se realizó en las bases de datos de Medline, Lilacs y SciELO. Se incluyeron artículos originales y revisiones narrativas publicadas entre 2020 y 2025 en inglés y español. Estudios demostraron que la higiene de manos y la limpieza ambiental rigurosa son esenciales para reducir la transmisión de *Clostridioides difficile*. La gestión efectiva requiere un enfoque integral que incluye el uso de esporicidas, la administración adecuada de antimicrobianos y la capacitación del personal de salud.

Palabras clave

Clostridioides difficile, Higiene de las Manos, Infección Hospitalaria, Epidemiología.

Introduction

Clostridioides difficile (*C. difficile*), formerly known as *Clostridium difficile*, is a Gram-positive, obligate anaerobic, spore-forming bacillus. It was discovered in 1935 in the fecal microbiota of healthy newborns. Today, it poses a challenge in various healthcare settings, especially in nursing homes and rehabilitation centers.ⁱ⁻ⁱⁱⁱ

C. difficile infection is a significant problem due to the bacterium's ability to cause infections ranging from mild, usually diarrhea, to severe, such as pseudomembranous colitis, which can be fatal.^{iv,v} Hospital-acquired *C. difficile* infection is currently the most prevalent and costly healthcare-associated infection (HAI) and represents a significant threat to patient safety worldwide.^{vi,vii}

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Estrategias de higiene integral frente a infecciones asociadas a la atención sanitaria por *Clostridioides difficile*

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HAIs can often originate from the patient's flora, altered by hospital pathogens transmitted by healthcare personnel or present in the environment. It is difficult to determine the source of infection, although some bacteria are more likely to be transmitted from the patient's environment; generally, thorough investigations are reserved for unusual cases or outbreaks in well-equipped hospitals.^{viii}

According to the World Health Organization, approximately 16 million people worldwide die each year from healthcare-associated infections. Of these deaths, about 17 % are attributed to people infected with *C. difficile*. This figure highlights the severity of infection with this microorganism and its impact on global mortality.^{ix}

Although hand hygiene has reduced HAIs over the past 25 years, a proportion remains that requires attention, and hospital environmental hygiene could be key.^{viii} *C. difficile* infection acquired in healthcare facilities in patients over 18 years of age is defined as infections diagnosed after at least three days of hospitalization, resulting from both community and hospital-acquired transmission.^{xi}

Several factors influence the severity of *C. difficile* infections. First, the epidemiology of *C. difficile* has changed in the last two decades, mainly due to the emergence of hypervirulent and antimicrobial-resistant strains, which have led to an increase in the incidence of severe infections, frequent outbreaks, and new risk factors.^{i,vii,xii} Second, the resistance of *C. difficile* spores to adverse conditions, such as heat, disinfectants, and antimicrobials, facilitates their transmission and survival in hospital settings, exacerbating the problem.^{ix,xiii} Finally, *C. difficile* infection is the leading cause of antibiotic-associated diarrhea,^{ix,xiv,xv} highlighting the need to implement appropriate policies for the rational use of antimicrobials and infection control practices to prevent its spread.

This narrative review was based on a search of the Medline, Lilacs, and SciELO databases, using the MeSH terms "*Clostridioides difficile*," "Hand Hygiene," "Cross Infection," and "Epidemiology," as well as the DeCS terms "*Clostridioides difficile*," "Higiene de las Manos," "Infección Hospitalaria," and "Epidemiología." The inclusion criteria considered a study population of hospitalized patients and healthcare personnel of all ages. Original articles and narrative reviews published between 2020 and 2025 in English and Spanish were included. Evidence was selected according to critical reading guidelines, and case reports, opinion articles, and editorials were

excluded. The main objective of this review was to synthesize the available evidence on healthcare-associated *C. difficile* infections and the comprehensive hygiene strategies that have been described for their prevention and control.

Discussion

Changing epidemiology

Since 1981, there have been publications on efforts to mitigate the risk of *C. difficile* transmission within healthcare settings, due to its relationship with patient safety and quality of healthcare. This leads to an increase in healthcare costs.^{vi}

C. difficile infection has been a growing concern for healthcare systems due to its increasing incidence in hospital and outpatient settings worldwide.^{ii,xvi} This has raised concerns about the mortality associated with *C. difficile* infection and its economic burden on healthcare systems.^{xvi-xviii} This is especially true given the recent association between chronic *C. difficile* and colon cancer.^{xix}

In German hospitals, *C. difficile* infection has declined, possibly due to social distancing practices implemented before the COVID-19 pandemic.^{xvi} In the United States, the pandemic contributed to fewer hospitalizations, which may have reduced nosocomial infections.^{xvi} Despite evidence that *C. difficile* was a significant problem for patients with COVID-19,^{xx} the burden of the infection increased even more in regions with low and medium development indices.^{xxi} The heterogeneity of strain virulence and its varied geographical distribution^{xxii} does not allow it to be linked to the rise of the pandemic, according to Hilvers *et al.*, other factors have probably influenced its increase since 2020.^{xxiii} The epidemiology of *C. difficile* has evolved, and it is estimated that 40 % of patients with community-associated infection require hospitalization.^{xxiv}

Strategies and vaccines for its prevention are currently being developed; however, the importance of hand hygiene and patient isolation as control measures is emphasized.ⁱⁱ The downward trends in Germany and the United States are primarily attributed to the pandemic, as hand hygiene and hospital control measures increased; however, these protective measures against COVID-19 do not fully explain the change in epidemiology, as the reverse trend had begun in 2015.^{xvi} Despite this, *C. difficile* infection continues to pose a challenge in global healthcare.^{xvi}

Risk factors and susceptibility

Antibiotic use is the main predisposing factor, as it alters the intestinal microbiota, facilitating colonization and allowing *C. difficile* to proliferate. Susceptibility to this infection varies according to the type, spectrum, duration, and amount of antibiotics used; prolonged and frequent use can increase vulnerability to infection. In hospitals, less than 35 % of symptomatic cases are related to previous cases. Stephenson *et al*, identified that 19.6 % of the total number of resistant patients admitted were possibly colonized during hospitalization.^{xxiv}

Resilience of spores

C. difficile spores, due to their remarkable ability to adapt and survive in adverse conditions within a hospital environment, pose enormous difficulties for the effective decontamination of surfaces and equipment.^{ix} Although studies have reported a decrease in hospital-acquired *C. difficile* infections during outbreaks when replacing non-sporicidal disinfectants with diluted bleach, environmental transmission of spores in endemic settings remains a persistent challenge.^{vi}

Colonized patients shed spores in their feces, contaminating surfaces and turning healthcare workers into vectors of transmission when they do not comply with contact precautions. Consequently, increased compliance with measures by healthcare personnel was the most effective intervention in reducing colonization, with reductions in HAs of up to 56 %.^{xxiv}

Prevention and control strategies

Prevention requires a comprehensive approach, as routine cleaning is not sufficient to eliminate spores. Rigorous disinfection procedures and the use of specific sporicidal agents are necessary. In addition, the complexity of medical equipment and the numerous surfaces in a hospital increase the challenge, as each area must be meticulously treated to prevent the spread of infections.^{vi,xxv}

The limited effectiveness of individual interventions suggests the need for a multifaceted approach to control these infections effectively.^{xxvi,xxvii} It is essential to adopt integrative and holistic strategies in hospital settings to address this challenge, which involves combining multiple tactics to improve disease prevention and management.

Comprehensive approach to hygiene techniques

Effective management of *C. difficile* infections requires a comprehensive approach because the presence of *C. difficile* spores requires multiple interventions in hygiene and infection control practices, ongoing staff training in advanced disinfection techniques, and the implementation of strict cleaning policies. It is essential to adopt preventive strategies, such as contact precautions, hand hygiene, efficient environmental cleaning, use of sporicidal agents, and rational antimicrobial stewardship policies. This is crucial to managing and minimizing the impact of *C. difficile* infection on public health.^{iv,v,xxv}

There are differences in scientific research regarding which of these interventions is most effective; some studies suggest that hand hygiene outperforms environmental cleaning,^{xxiv} while others indicate the opposite.^{xxiv,xxviii} *C. difficile* transmission can occur both through contact with contaminated surfaces and through the hands of healthcare personnel, highlighting the connection between the environment and personal hygiene practices. Agent-based transmission models indicate that the sequence of transmission events may influence the relative effectiveness of environmental versus personal interventions.^{xxiv}

Hand hygiene

Hand hygiene is one of the most cost-effective measures for preventing the transmission of *C. difficile*.^{xvii,xxviii} Despite this, in recent years, hand hygiene initiatives have not reduced pathogens as expected, yet they are critical to preventing the transmission of infections in healthcare settings.^{xxi}

Although it is difficult to measure the exact risk, evidence suggests that the hands of healthcare workers are a significant route of transmission.^{xxv}

Uncontaminated surfaces do not transmit pathogens, even without hand hygiene, so environmental and hand hygiene should be considered interdependent and essential for preventing infections.^{xxix}

Hand hygiene is economical and effective, with studies showing a return of \$32.73 (in 2018) for every dollar invested. This is profitable even with less than a 1 % reduction in infections.^{xvii,xviii}

Studies conducted in the Slovak Republic and Malawi evaluated hygienic handwashing practices and adherence.^{xxx,xxxi} In Slovakia, one-third of students did not adequately comply with the handwashing techniques recommended by the World

Health Organization. However, no significant differences in microbial contamination were detected between those who followed the protocols and those who did not comply. In the study conducted in Malawi, involving clinicians and medical students, low adherence to hand hygiene practices was observed, mainly due to forgetfulness and negligence. To improve compliance, a comprehensive hospital approach is proposed, including education for physicians and students, the use of alcohol-based disinfectants, visual reminder posters, and examples set by experienced professionals for younger ones.

Environmental cleaning

Environmental cleaning is a key strategy for preventing HAIs.^{xxxii} It includes strategies ranging from the careful selection of cleaning products and methods, considering patient risk profiles, surfaces, and pathogens, to the application of cleaning techniques involving steps such as visual assessment, area preparation, cleaning, and drying.^{xxxiii} Cleaning involves the manual removal of impurities such as grease and dirt from specific surfaces, typically using a cloth or towel together with soap or detergent.^{xxxiii}

On the other hand, disinfection seeks to eliminate or reduce the presence of harmful microorganisms on surfaces. It is most effective when performed after cleaning, which has physically removed pathogens. It is crucial to avoid cross-contamination by changing clothes between rooms and contact areas.^{xxxiii} Staff education and training are critical to the success of interventions, as are auditing and timely feedback to maintain infection control practices.^{xxxiii} Effective communication is vital for engaging staff and supporting a change in organizational culture. The importance of environmental services staff in patient safety must also be recognized.^{viii, xxxiii, xxxiv}

Strategic approaches to environmental hygiene

Wenzel and Edmonds highlighted the crucial role of environmental hygiene as an essential component in strategies to prevent HAIs.^{xxxv} Two approaches are mentioned: “horizontal interventions,” which address a wide range of infectious threats in healthcare settings, and “vertical interventions,” which focus specifically on particular pathogens or conditions.^{vi} The main difference between these approaches lies in their scope: while vertical interventions are more specific and targeted, horizontal inter-

ventions have a more widespread impact. The latter aspect is particularly relevant in endemic settings, where infection prevention is a constant concern. The distinction between these modalities highlights the importance of implementing a multifaceted approach to HAIs prevention and underscores the critical role that horizontal interventions play in effectively addressing diverse infectious threats.^{vi}

Spore-killing agents

Given the resistance of *C. difficile* spores, conventional disinfectants are insufficient, making it crucial to develop new sporicidal agents that can be used daily without damaging surfaces, equipment, or the environment.^{vi} These innovations, combined with programs aimed at optimizing cleaning and disinfection, have the potential to significantly reduce hospital-acquired *C. difficile* infections.^{xxxv} In addition, improvements in environmental and hand hygiene can contribute significantly to patient safety by reducing the acquisition of spores and other environmentally transmitted pathogens.^{vi, xxxv}

Hand hygiene strategies and environmental cleaning products can vary widely between institutions and regions, making it difficult to generalize results and identify best practices.^{xxxvi}

The multimodal approach includes multiple interventions and must be comprehensive, considering both environmental elimination of the pathogen and reduction of patient risk factors, as well as practical application and staff training. The success of HAIs prevention through horizontal and vertical interventions, complemented by sporicidal agents, depends on both their design and implementation.

A study was implemented in a tertiary hospital in Australia to improve environmental hygiene and reduce HAIs transmission.^{xxxvii} Over six months, a study in Spain did not show a statistically significant reduction in HAI transmission rates. However, it did show a significant improvement in cleaning performance, as measured by UV markers.^{xxxviii}

The results suggest that this multimodal approach may have a positive long-term impact on reducing the risk of cross-transmission. In addition, the study highlights the importance of considering contextual factors when implementing changes in hospital hygiene practices. It emphasizes the need to adequately train environmental services staff to improve cleaning performance.^{xxxv}

It was also observed that specific training improved the knowledge and attitudes of

environmental services staff, suggesting that professional development and interdisciplinary cooperation are crucial for long-term success in preventing IAAS.^{xxxv}

Current perspectives incorporate the use of artificial intelligence to identify patients at risk. For example, research conducted by Tang et al, used an AI-guided model to prioritize preventive efforts. When comparing the results before and after using this tool, although the incidence of *C. difficile* was not reduced, the use of certain antibiotics associated with a higher risk of infection was reduced.^{xxxix} Although there are inherent limitations to this type of design and a possible risk of selection bias or exclusion of relevant studies, it was possible to identify the importance of a multimodal approach to infection prevention in the hospital setting.

Conclusion

Clostridioides difficile infection represents a priority challenge for public health and patient safety in hospital settings. Its epidemiology has changed over the last decade, and its control is conditioned by the widespread use of antibiotics and the high environmental resistance of spores. In this context, the implementation of comprehensive prevention strategies is essential. A multimodal approach that combines hand hygiene, environmental cleaning, and disinfection with sporicidal agents, along with ongoing education for healthcare personnel and antibiotic optimization programs, has been shown to improve the quality of control practices and reduce the risk of cross-transmission. The sustained success of these interventions requires not only the systematic application of standardized hygiene packages but also interdisciplinary collaboration, institutional commitment, and ongoing training. Together, these factors enable progress toward safer and higher-quality care.

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