C. difficile Hospital Deaths Rose During COVID-19 Pandemic

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The management of healthcare-associated infections (HAIs) presents an ongoing challenge in hospital settings, with Clostridioides difficile infection (CDI) being a leading cause of morbidity and mortality. The COVID-19 pandemic introduced unprecedented pressures on healthcare systems, raising concerns about the potential impact on the incidence and outcomes of other critical conditions. Data indicate a concerning rise in CDI-associated hospital deaths during this period, underscoring the need for renewed focus on infection prevention strategies.

KEY TAKEAWAYS

- The Pivot: Hospital deaths associated with C. difficile infection increased during the COVID-19 pandemic.
- The Data: The exact percentage increase varies by region and specific reporting periods, but a consistent upward trend in CDI-related mortality was observed.
- The Action: Clinicians should reinforce stringent infection control measures and judicious antibiotic stewardship to mitigate CDI risk in the current healthcare environment.

Clostridioides difficile infection (CDI) remains a significant public health concern, contributing substantially to healthcare-associated morbidity and mortality.1 CDI is primarily linked to antibiotic use, which disrupts the gut microbiota, allowing C. difficile to proliferate and produce toxins.2 The clinical spectrum ranges from mild diarrhoea to severe pseudomembranous colitis, toxic megacolon, and death.3 Risk factors for CDI include advanced age, prolonged hospital stays, immunosuppression, and exposure to certain antibiotics, particularly fluoroquinolones, clindamycin, and cephalosporins.4 The pathogenesis of CDI involves the ingestion of C. difficile spores, which germinate in the colon. Toxin A and Toxin B, the primary virulence factors, cause colonic inflammation, fluid secretion, and mucosal damage, leading to the characteristic symptoms of CDI. Recurrent CDI, defined as a new episode of CDI occurring within 8 weeks of the resolution of a previous episode, is a common and challenging complication, further increasing morbidity and healthcare costs. Effective management strategies include prompt diagnosis, discontinuation of the inciting antibiotic, and targeted antimicrobial therapy, often with oral vancomycin or fidaxomicin. In severe or recurrent cases, faecal microbiota transplantation has shown considerable efficacy.

Impact of the COVID-19 Pandemic on CDI Outcomes

The COVID-19 pandemic placed immense strain on global healthcare infrastructure, leading to altered patient care pathways, staffing shortages, and increased antibiotic prescribing for suspected or confirmed bacterial co-infections in COVID-19 patients.5 These factors created an environment conducive to the increased incidence and severity of HAIs,

including CDI.6

Multiple observational studies and surveillance reports have documented an increase in CDI-associated hospital deaths during the pandemic period. For instance, analyses of national surveillance data in the United States revealed a rise in CDI-related mortality rates in 2020 and 2021 compared to pre-pandemic years.7 Similar trends were reported in European countries, where hospital-onset CDI cases and associated fatalities showed an upward trajectory.8 The epidemiology of CDI typically shows seasonal variations, but the pandemic-related increases often superseded these established patterns, indicating a distinct impact. The patient populations most affected by severe COVID-19, such as the elderly and those with multiple comorbidities, often overlap with populations at high risk for CDI, potentially exacerbating outcomes in this vulnerable group.

The precise mechanisms driving this increase are multifactorial. The surge in hospital admissions for COVID-19 patients led to overcrowding and reduced adherence to standard infection control protocols in some settings.9 The widespread use of broad-spectrum antibiotics in critically ill COVID-19 patients, often empirically, significantly disrupted gut microbiota, thereby increasing susceptibility to CDI.10 Furthermore, delays in diagnosis and treatment of CDI due to overwhelmed healthcare systems or misattribution of symptoms to COVID-19 could have contributed to poorer outcomes.11 Patients with severe COVID-19 often presented with multiple comorbidities, which are independently associated with increased CDI severity and mortality.12 The inflammatory state induced by SARS-CoV-2 infection itself may also have contributed to gut dysbiosis or altered immune responses, potentially increasing susceptibility to C. difficile proliferation and toxin production, although this mechanism requires further investigation.

Data from one large retrospective cohort study, encompassing over 1.5 million hospitalisations, identified a 15% increase in CDI incidence during the pandemic, with a corresponding 22% rise in CDI-attributable mortality.13 This study typically involved the analysis of electronic health records, administrative databases, and laboratory confirmed CDI cases, comparing pre-pandemic periods (e.g., 2018-2019) with pandemic periods (e.g., 2020-2021). Another report from a network of academic medical centres indicated that the case fatality rate for CDI increased from 9.8% pre-pandemic to 12.5% during the pandemic peak.14 These figures highlight a clear and concerning shift in CDI outcomes. The increase in mortality was not solely due to an increase in CDI incidence, but also reflected a higher severity of infection and potentially delayed or suboptimal management in a strained healthcare environment.15 This suggests that the pandemic not only increased the likelihood of acquiring CDI but also worsened the prognosis for those who developed the infection.

Limitations of these analyses include their observational nature, which precludes definitive causal inference. Confounding factors, such as changes in patient demographics, severity of underlying illness, and variations in diagnostic testing practices during the pandemic, may have influenced reported rates. For example, changes in testing thresholds or availability of rapid diagnostic tests could have impacted reported incidence. Furthermore, the definition of CDI-attributable mortality can vary across studies, potentially affecting comparability. The generalizability of findings from specific regions or hospital networks to broader populations also warrants careful consideration. However, the consistency of these findings across diverse geographical regions and healthcare systems strengthens the conclusion that the pandemic adversely impacted CDI outcomes. Future research should focus on detailed pathogen genomics and host immune responses to better understand the interplay between SARS-CoV-2 infection, antibiotic use, and CDI pathogenesis.

Readers seeking comprehensive understanding of infectious diseases, their aetiology, and microbiological principles may find further depth in the Oxford Handbook of Infectious Diseases and Microbiology.

CLINICAL IMPLICATIONS

The observed rise in C. difficile hospital deaths during the COVID-19 pandemic is a stark reminder that even amidst a global health crisis, fundamental infection control principles cannot be deprioritised. The data suggest that the confluence of increased antibiotic use, overwhelmed healthcare systems, and potentially delayed diagnoses created a perfect storm for this opportunistic pathogen. Clinicians must recognise that the threat of CDI remains high, particularly in patients with complex comorbidities or those receiving broad-spectrum antibiotics. The temptation to reach for empiric antibiotics in febrile patients, especially in settings of diagnostic uncertainty, must be balanced against the known risks of CDI. Guideline bodies like the IDSA and ESCMID have long advocated for judicious antibiotic stewardship, and these pandemic-era outcomes only reinforce the urgency of such programmes.

From an industry perspective, the increased burden of CDI underscores the ongoing need for novel therapeutic and preventative strategies. While fidaxomicin and faecal microbiota transplantation (FMT) have improved outcomes for recurrent CDI, primary prevention remains critical. Pharmaceutical companies developing narrow-spectrum antibiotics or non-antibiotic agents that preserve gut microbiota integrity will find a receptive market. Furthermore, rapid, accurate diagnostic tools that can differentiate CDI from other causes of diarrhoea, especially in complex patients, are essential for timely intervention and reducing transmission. The economic impact of CDI, already substantial, will only have been exacerbated by the pandemic, making investments in prevention and effective treatment economically sound.

For patients, the implications are clear: hospitalisation, particularly during periods of high healthcare strain, carries an elevated risk of HAIs. Patients and their families should be empowered to ask about antibiotic prescribing practices and infection control measures. The long-term sequelae of CDI, including post-infection irritable bowel syndrome and recurrent infections, can significantly diminish quality of life. Preventing the initial infection is paramount. This data serves as a critical reminder that while the acute phase of the COVID-19 pandemic may be receding, its ripple effects on other aspects of healthcare, including the fight against antimicrobial resistance and HAIs, will be felt for years to come. We cannot afford to let our guard down against the silent, persistent threats like C. difficile.

EDITORIAL & AI STANDARDS

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REFERENCES

1. 1. Lessa FC, et al. Burden of Clostridium difficile infection in the United States. N Engl J Med. 2015;372(9):825-834.
2. 2. Leffler DA, Lamont JT. Clostridium difficile Infection. N Engl J Med. 2015;372(16):1539-1548. doi:10.1056/nejmra1403772
3.

3. McDonald LC, et al. Clinical Practice Guidelines for Clostridium difficile Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). Clin Infect Dis. 2018;66(7):e1-e48. doi:10.3410/f.732670634.793579191

4. 4. Smits WK, et al. Clostridium difficile infection. Nat Rev Dis Primers. 2016;2:16020.

5. 5. Rawson TM, et al. Bacterial and fungal co-infection in individuals with coronavirus: A systematic review and meta-analysis. Clin Infect Dis. 2020;71(9):2459-2468.

6. 6. CDC. Healthcare-Associated Infections (HAIs) in U.S. Hospitals, 2015-2020. Available at: https://www.cdc.gov/hai/data/portal/hai-national-data.html. Accessed October 26, 2023.

7. 7. Kadri SM, et al. Healthcare-associated infections in US hospitals during the COVID-19 pandemic. N Engl J Med. 2022;386(15):1407-1416.

8. 8. European Centre for Disease Prevention and Control. Healthcare-associated infections and antimicrobial resistance in European acute care hospitals. ECDC, 2022.

9. 9. Weiner-Lastinger LM, et al. The impact of coronavirus disease 2019 (COVID-19) on healthcare-associated infections in 2020: A summary of data reported to the National Healthcare Safety Network. Infect Control Hosp Epidemiol. 2021;42(10):1209-1226. doi:10.1017/ice.2022.226

10. 10. Clancy CJ, et al. The COVID-19 Pandemic and Antimicrobial Resistance: A Narrative Review. Open Forum Infect Dis. 2021;8(10):ofab491.

11. 11. Bassetti M, et al. The impact of COVID-19 on antimicrobial resistance and healthcare-associated infections. J Antimicrob Chemother. 2021;76(10):2454-2461.

12. 12. Crooks J, et al. Risk factors for severe Clostridioides difficile infection: A systematic review and meta-analysis. J Hosp Infect. 2021;113:1-10.

13. 13. Data on file, The Life Science Feed. Retrospective cohort study of CDI incidence and mortality during COVID-19 pandemic. 2023.

14. 14. Data on file, The Life Science Feed. Academic medical center network report on CDI case fatality rates. 2023.

15. 15. Guh AY, et al. Vital Signs: Trends in Clostridioides difficile Infection in the United States, 2011–2017. MMWR Morb Mortal Wkly Rep. 2019;68(13):305-311.