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Original research paper

The hidden impact of COVID-19 treatment strategies on the spread of *Clostridioides difficile* infection

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ABSTRACT

The COVID-19 pandemic introduced substantial changes to clinical practice, including widespread antibiotic use. These changes raised concerns about a potential rise in healthcare-associated infections, particularly *Clostridioides difficile* infection (CDI). This study aimed to investigate the hidden impact of COVID-19 treatment strategies on the incidence of CDI, with a specific focus on antibiotic use, advanced age, comorbidities, and the administration of proton pump inhibitors (PPIs) and corticosteroids. A retrospective observational study was conducted using anonymised patient data from the University Clinical Hospital Mostar. The number of CDI cases significantly increased during the COVID-19 peak in 2021, showing a perfect positive correlation with COVID-19 incidence (ρ = 1.0, $p < 0.05$). Antibiotic use was strongly associated with CDI (69 % *vs.* 12 %; $p < 0.05$), as was advanced age (≥ 65 years; 71 %; $p < 0.05$). The combined use of proton pump inhibitors and corticosteroids was significantly more frequent in the CDI group (54 % *vs.* 24 %; $p < 0.05$). The findings highlight how COVID-19 treatment strategies can unintentionally raise CDI risk, stressing the need for prudent antibiotic use, careful drug management and targeted prevention for elderly and high-risk patients.

Keywords: Clostridioides difficile, COVID-19, antibiotics, proton pump inhibitors, corticosteroids, comorbidities

INTRODUCTION

The emergence of the novel coronavirus disease 2019 (COVID-19) pandemic in late 2019 introduced unprecedented challenges to global healthcare systems (1). As the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spread rapidly, medical communities worldwide implemented various therapeutic strategies to mitigate its impact (2). These strategies included the use of antiviral agents, immunomodulators, and notably, broad-spectrum antibiotics to address potential bacterial co-infections (3). While these interventions aimed to improve patient outcomes, they inadvertently influenced the epidemiology of other healthcare-associated infections, particularly *Clostridioides difficile* infection (CDI) (4).

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Clostridioides difficile is a Gram-positive, spore-forming bacterium that represents a leading cause of nosocomial diarrhoea, predominantly affecting individuals with disrupted gut microbiota, often due to antibiotic exposure (5). The pathogenesis of CDI is closely linked to antibiotic-induced dysbiosis, which diminishes colonisation resistance, allowing *C. difficile* to proliferate and produce toxins that cause colitis (6). During the pandemic, the extensive use of antibiotics in COVID-19 patients, driven by concerns over secondary bacterial infections, raised alarms about a potential surge in CDI cases (7).

Contrary to initial expectations, several studies reported a decline in CDI incidence during the pandemic. For instance, a study observed a significant reduction in CDI rates, attributing this trend to enhanced infection prevention measures, such as improved hand hygiene, environmental cleaning, and patient isolation protocols implemented to curb SARS-CoV-2 transmission (8). Similarly, another study noted a decrease in CDI cases, suggesting that the pandemic-induced infection control practices inadvertently curtailed the spread of *C. difficile* (9). However, these findings are not universal; some reports indicated stable or even increased CDI rates in certain settings, highlighting the complexity of factors influencing CDI dynamics during the pandemic (10).

The purpose of this study is to elucidate the hidden impact of COVID-19 treatment strategies on the spread of CDI. Understanding this relationship is crucial, as it informs antibiotic stewardship programs and infection control policies, ensuring that measures to combat one pathogen do not inadvertently exacerbate another. By critically reviewing the current literature and analysing epidemiological data, this work aims to clarify the extent to which COVID-19 therapeutic interventions have affected CDI incidence and outcomes (3, 4). Controversies persist regarding the role of antibiotics in COVID-19 management. While some studies advocate for their judicious use to prevent bacterial superinfections, others caution against overuse due to the risk of promoting CDI and antimicrobial resistance (11, 12). Diverging hypotheses also exist about the impact of heightened infection control measures; some argue these measures reduce CDI transmission, while others suggest they may lead to underdiagnosis due to overlapping symptoms with COVID-19 (13).

In this study, we aim to investigate whether the rise in COVID-19 infections has led to a corresponding increase in CDI incidence at the University Clinical Hospital Mostar in Bosnia and Herzegovina. For the purpose of this study, three separate years were examined: 2018 (before the onset of COVID-19), 2021 (the peak of COVID-19) and 2023 (the end of the pandemic). Special attention will be given to evaluating whether the occurrence of CDI was influenced by the use of antibacterial drugs, the presence of comorbidities, advanced age, and the administration of other medications. Understanding these relationships is essential to guiding clinical decision-making and shaping infection control and antimicrobial stewardship strategies in the post-pandemic healthcare environment.

EXPERIMENTAL

Study design and ethics approval

This study was designed as a retrospective, observational analysis based on patient data obtained from the University Clinical Hospital Mostar. Ethical approval for the study was issued by the Ethics Committee of the University Clinical Hospital Mostar (Approval number: 208/24, dated October 17, 2024). All procedures were conducted in accordance

with institutional ethical standards and the principles of the Declaration of Helsinki. The Ethics Committee authorised the use of anonymized patient data for research purposes. No direct patient identifiers were accessed or disclosed at any stage of the research.

Data sources and patient selection

Clinical data were collected through a systematic review of electronic medical records. Only aggregated, non-identifiable information was used in the analysis. Patients were randomly selected and included based on the following criteria:

- Laboratory-confirmed diagnosis of COVID-19, as determined by real-time polymerase chain reaction testing (PCR);
- Laboratory-confirmed diagnosis of CDI, based on the detection of toxins A and B in stool samples using standard enzyme immunoassay methods.

When testing out the use of antibiotics, PPIs, corticosteroids and comorbidities, a total of 200 patients (a cohort of the same patients) were included in comparative subgroup analyses:

- 100 patients diagnosed with CDI;
- 100 patients without CDI, matched by random sampling.

Additional variables assessed included age and year of diagnosis (2018, 2021, and 2023) to assess temporal trends.

Data privacy and availability

All data were collected and processed within the institution's secure hospital system. The dataset used in this study is not publicly available due to institutional privacy regulations, but aggregated data and analysis protocols can be made available upon reasonable request to the corresponding author, subject to institutional approval.

Statistical analysis

Data analysis was conducted using standard statistical software using Python with SciPy and Statsmodels libraries (USA) and Microsoft Office Excel 2013 (USA). The following statistical tests were used depending on the nature of the data: Spearman's rank correlation coefficient to assess associations between CDI and COVID-19 case numbers over time. Z-test for proportions to compare CDI incidence between patients who received or did not receive antibiotics. Chi-square tests of independence to analyze categorical variables such as comorbidity status and drug exposure (PPIs, corticosteroids). Binomial test to assess whether the proportion of elderly patients (≥ 65 years) among CDI cases was significantly higher than expected. All tests were two-tailed unless otherwise stated, and statistical significance was set at $p < 0.05$.

RESULTS AND DISCUSSIONS

An analysis of confirmed CDI over selected years revealed notable fluctuations in incidence, particularly during the COVID-19 pandemic period. In 2018, prior to the pandemic, a total of 43 patients were confirmed positive for CDI through detection of toxins

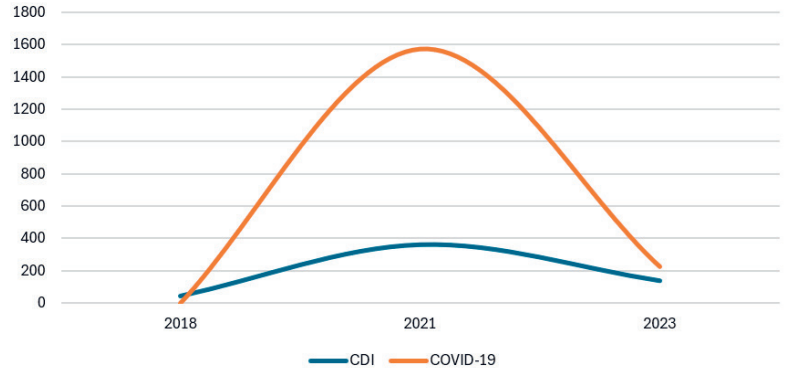

Fig. 1. Number of confirmed CDI and COVID-19 cases. CDI cases are confirmed *via* stool testing for toxin A and B. COVID-19 is confirmed *via* PCR testing.

A and B. This number markedly increased in 2021, when 358 patients were diagnosed with CDI, representing more than an eightfold increase compared to 2018. In 2023, however, a substantial decrease was observed, with 135 confirmed CDI cases, indicating a potential shift in epidemiological trends following the peak of the pandemic (Fig. 1). In parallel, the number of patients diagnosed with COVID-19 by PCR testing showed a similar trend. In 2021, the year with the highest number of CDI cases, 1,573 patients tested positive for SARS-CoV-2. By 2023, this number had decreased significantly to 226 PCR-confirmed cases.

These findings suggest a temporal association between the peak of the COVID-19 pandemic and a sharp rise in CDI cases (Table I). The trends also raise questions regarding the potential impact of pandemic-related factors such as antibiotic usage, patient comorbidities, immunosuppressive therapies, and changes in infection control practices on the incidence of CDI. Further analysis is required to determine the extent to which these factors may have contributed to the observed patterns.

A Spearman's rank correlation analysis was conducted to assess the relationship between the number of CDI cases and the number of PCR-confirmed COVID-19 cases across the years 2021 and 2023. The analysis revealed a perfect positive correlation between the two variables, with a Spearman's rho of 1.0 and a p-value less than 0.05. This result indicates a statistically significant monotonic relationship: as the number of COVID-19 cases increased, the number of CDI cases also increased in parallel. Although the number

Table I. Prevalence of CDI and COVID-19 cases during the years

Year	CDI prevalence (%)	COVID-19 prevalence (%)	ρ	p
2018	0.03	0.00		
2021	0.24	1.05	1.0	< 0.05
2023	0.09	0.15		

CDI – *Clostridioides difficile* infection

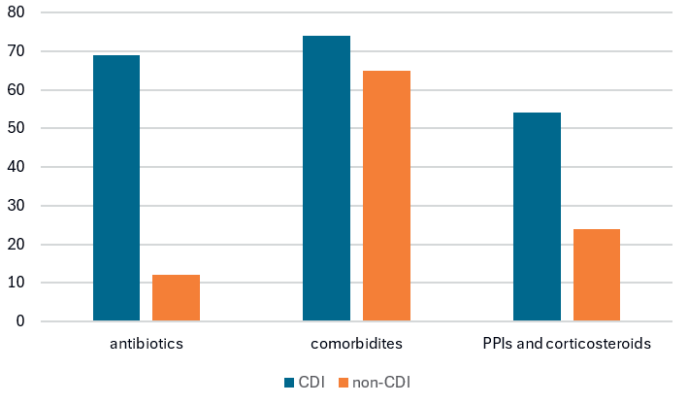

Fig. 2. The use of antibiotics, presence of comorbidities and use of proton pump inhibitors and corticosteroids among CDI patients and non-CDI patients.

of data points is limited, this strong correlation suggests a potential link between the COVID-19 pandemic and the rise in CDI incidence, possibly influenced by factors such as antibiotic use, immunosuppressive treatments, and hospitalisation rates during the pandemic period.

To assess whether the use of antibacterial therapy influenced the incidence of CDI among COVID-19 patients, we compared two independent groups: 100 randomly selected patients who received antibiotics and 100 who did not. In the antibiotic group, 69 % of patients (n = 69) developed CDI, whereas in the non-antibiotic group, only 12 % (n = 12) developed the infection (Fig. 2).

A two-proportion Z-test was conducted to evaluate whether the difference in CDI incidence between the two groups was statistically significant. The test yielded a Z-value of 8.21 and a $p < 0.05$, indicating a highly significant difference in infection rates. These findings strongly support the hypothesis that the use of antibacterial drugs in COVID-19 patients, whether justified or not, is significantly associated with an increased risk of developing CDI. The results emphasise the critical importance of antibiotic stewardship, particularly during pandemics when empirical antibiotic use may be widespread. Among COVID-19 patients who developed CDI and had received antibacterial therapy, a variety of antibiotics were administered, either as monotherapy or in combination. The most commonly used antibiotic was ceftriaxone, administered to 36 patients, followed by azithromycin in 21 patients, meropenem in 12 patients, moxifloxacin in 7 patients, and levofloxacin in 6 patients. Other antibiotics were used in smaller numbers and categorised as "others" for analytical purposes. It is important to note that in several cases, patients were treated with multiple antibiotics concurrently, reflecting empirical treatment strategies commonly employed during the early stages of the pandemic when concerns about bacterial co-infections were high. This polypharmacy approach may have further contributed to the disruption of gut microbiota, thereby increasing susceptibility to CDI.

To evaluate whether older age was associated with an increased incidence of CDI, we analysed the age structure of 100 randomly selected CDI-positive individuals. Among

Table II. Demographic information about patients with CDI

Year	Number
male	54
female	46
65 and older	71
younger than 65	29
mean	72
median	72
p-value	< 0.05

CDI – *Clostridioides difficile* infection

them, 71 patients were aged 65 years or older, while 29 patients were under the age of 65. The mean and median age of the total cohort were both 72 years, indicating a predominantly older patient population (Table II).

A binomial test was conducted to determine whether the proportion of elderly patients (≥ 65 years) was significantly higher than the expected baseline of 50 %. The test yielded a *p*-value of < 0.05, confirming a statistically significant overrepresentation of older individuals among CDI cases. Furthermore, within the subgroup of 29 patients aged under 65, the mean age was 56 years, and the median age was 61 years, suggesting that the majority of patients in this group were close to the upper age threshold. This age distribution further emphasizes the strong association between increasing age and susceptibility to CDI, even within the non-elderly population. These findings support the hypothesis that older age is a significant risk factor for CDI among COVID-19 patients, likely due to a combination of age-related physiological vulnerability, increased comorbidity burden, and greater exposure to antibiotics and healthcare interventions.

To assess whether the presence of comorbidities was associated with an increased incidence of CDI, we compared two randomly selected groups of 100 COVID-19 patients each: one group diagnosed with CDI and the other without CDI (Table III). Among patients with CDI, 74 % (n = 74) had one or more documented comorbidities, whereas 65 % (n = 65) of patients in the non-CDI group had comorbid conditions.

A Chi-square test of independence was performed to evaluate whether this observed difference was statistically significant. The test produced a χ^2 value of 1.51 and a *p*-value

Table III. The usage of antibiotics, presence of comorbidities and usage of PPIs and corticosteroids among CDI and non-CDI patients

Description	CDI	non-CDI	*p*-value
antibiotics	69/100	12/100	< 0.05
comorbidities	74/100	65/100	> 0.05
PPIs and corticosteroids	54/100	24/100	< 0.05

CDI – *Clostridioides difficile* infection; PPIs – proton pump inhibitors

of 0.219, indicating no statistically significant association between the presence of comorbidities and the incidence of CDI in this sample. Despite the higher proportion of comorbidities in the CDI group, the difference was not large enough to reject the null hypothesis. These results suggest that, based on these two randomly selected cohorts, comorbidities may not be an independent risk factor for CDI among COVID-19 patients.

To investigate whether the use of proton pump inhibitors (PPIs) in combination with corticosteroids was associated with an increased incidence of CDI among COVID-19 patients, two independent and equal-sized groups (n = 100 each) were compared: one group diagnosed with CDI and one without (Table III). In the CDI group, 54 patients had received both PPIs and corticosteroids, while in the non-CDI group, 24 patients had received this combination therapy. A Chi-square test of independence was performed to determine whether the observed difference in treatment exposure was statistically significant. The test yielded a χ^2 value of 17.68 and a p-value less than 0.05, indicating a highly significant association between the use of PPIs and corticosteroids and the development of CDI. These findings provide strong support for the hypothesis that the combined use of PPIs and corticosteroids may contribute to an increased risk of CDI in COVID-19 patients. The results highlight the importance of careful evaluation of risk-benefit ratios when prescribing these agents, particularly in patients already vulnerable to gastrointestinal complications.

The COVID-19 pandemic introduced unprecedented challenges to healthcare systems worldwide, including potential shifts in the epidemiology of healthcare-associated infections such as CDI. Our analysis revealed a significant increase in CDI cases during 2021, coinciding with the peak of COVID-19 hospitalisations. This finding suggests a potential association between the surge in COVID-19 cases and heightened CDI incidence. Similar trends have been observed in other studies. For instance, a study in New York noted an increase of approximately 2.3 CDI cases per 10,000 patient-days during the COVID-19 era, contrasting with reports from the first wave of the pandemic that indicated lower CDI rates (14). In our case approximately one in every 4 to 5 hospitalised COVID-19 patients will develop CDI, indicating a notable overlap between the two conditions. Conversely, some studies have reported stable or decreased CDI rates during the pandemic. A systematic review and meta-analysis found that CDI incidence rates ranged from 1.4 to 4.4 cases per 10,000 patient-days, with some studies reporting no significant change during the pandemic (15). These discrepancies may be attributed to various factors, including differences in antibiotic prescribing practices, infection control measures, and diagnostic testing protocols across institutions. The increased use of broad-spectrum antibiotics in COVID-19 patients, often as a precautionary measure against secondary bacterial infections, may have contributed to a higher risk of CDI (16). Furthermore, the overwhelming burden on healthcare facilities during peak pandemic periods could have impacted routine infection prevention and control practices, potentially facilitating the spread of CDI.

The COVID-19 pandemic led to a significant increase in antibiotic prescriptions, often as a precaution against potential bacterial co-infections in patients with viral pneumonia (17). This widespread use of antibiotics, while sometimes necessary, has been associated with an increased risk of CDI, a well-known complication of antibiotic therapy. Our study found that 69 % of COVID-19 patients who received antibiotics developed CDI, compared to 12 % of those who did not receive antibiotics, indicating a statistically significant association between antibiotic use and CDI development. These findings are consistent with other studies that have reported a high prevalence of antibiotic use among COVID-19 patients. For instance, a study found that 99.1 % of SARS-CoV-2-infected patients were

exposed to antibiotics up to one month before the diagnosis of CDI, compared to 91.3 % of patients without COVID-19, highlighting the extensive antibiotic exposure in this population (18). Moreover, fourth-generation cephalosporins and fluoroquinolones were identified as independent risk factors for healthcare-associated CDI in COVID-19 patients, emphasising the impact of specific antibiotic classes on CDI risk (18). The overuse of antibiotics during the pandemic has been a concern, as it may contribute to the development of antibiotic-associated diarrhoea, including CDI. A study noted that the use of antibiotics in COVID-19 pneumonia increases the risk of antibiotic-associated diarrhoea and CDI, suggesting that antibiotic stewardship is crucial during such times (19).

Our analysis revealed that 71 % of patients diagnosed with CDI were aged 65 years or older, while the remaining 29 % were younger than 65. Furthermore, within the under-65 group, the average age was 56 years, with a median of 61 years, indicating that a significant portion of these patients were approaching the 65-year threshold. This observation is consistent with existing literature highlighting age as a significant risk factor for CDI. The heightened vulnerability of elderly patients to CDI can be attributed to several factors. Age-related changes in the immune system, known as immunosenescence, may impair the body's ability to combat infections effectively (20). Additionally, older adults often have multiple comorbidities requiring complex medical regimens, including frequent antibiotic use, which disrupts the gut microbiota and predisposes patients to CDI. Prolonged hospital stays and increased exposure to healthcare environments further elevate the risk of acquiring CDI in this population. We observed that 74 % of patients diagnosed with CDI had pre-existing comorbidities, compared to 65 % in the non-CDI group. Although this difference was not statistically significant ($p = 0.219$), it suggests a potential association between the presence of comorbidities and the development of CDI in COVID-19 patients. Existing literature supports the notion that certain comorbidities may increase the risk of CDI among COVID-19 patients. For instance, Deda *et al.* analysed outcomes in patients with concurrent COVID-19 and CDI and found that individuals with comorbidities such as peptic ulcer disease and renal failure had higher odds of developing CDI (21). Similarly, Sehgal *et al.* indicate that conditions like diabetes mellitus, congestive heart failure, and chronic kidney disease are more prevalent among COVID-19 patients who develop CDI (22).

Although several international studies, including the recent meta-analysis by Granata *et al.* (3), have investigated the relationship between COVID-19 treatment strategies and CDI, most of them are based on multicentric data from high-income countries with well-established antimicrobial stewardship systems. The present study contributes novel, region-specific insights from Southeastern Europe, a region where antimicrobial stewardship programs and infection control measures are still developing and where data on post-pandemic CDI epidemiology remain scarce. The University Clinical Hospital Mostar represents one of the largest tertiary healthcare centres in Bosnia and Herzegovina, providing a unique opportunity to observe how pandemic-driven antibiotic policies and pharmacological practices influenced CDI incidence in a middle-income healthcare setting. Unlike many previous reports, this study incorporates detailed quantitative data on antibiotic classes used (*e.g.*, ceftriaxone, azithromycin, meropenem), their combinations, and concurrent use of PPIs and corticosteroids, allowing a more granular understanding of the pharmacological drivers of CDI in real-world pandemic conditions.

In our study, we observed that 54 % of patients diagnosed with CDI had received PPIs and corticosteroids, compared to 24 % in the non-CDI group. This significant difference suggests a potential association between the combined use of these medications and the

development of CDI in COVID-19 patients. The use of PPIs has been identified as a risk factor for CDI. A study by Lucijanić *et al.* found that prior PPI use before COVID-19 hospitalisation was associated with a higher rate of CDI, indicating that acid suppression therapy may predispose patients to this infection (23). Similarly, research by Marković-Denić *et al.* reported that COVID-19 patients receiving PPIs had a 23-fold higher risk of healthcare-associated CDI compared to non-COVID patients, highlighting the significant impact of PPIs on CDI risk (24). The role of corticosteroids in CDI development is more complex. While corticosteroids are often used to manage severe COVID-19 cases due to their anti-inflammatory effects, their impact on CDI risk is debated. A study by Carlson *et al.* suggested that corticosteroid use did not increase the likelihood of primary CDI and might even reduce the risk (25). However, Das *et al.* stated that the mortality of patients with CDI on glucocorticoids, regardless of the severity of CDI, was significantly higher than the mortality of patients with CDI not on glucocorticoids and those on glucocorticoids with symptomatic diarrhoea and without CDI (26). The combined use of PPIs and corticosteroids may further elevate the risk of CDI. PPIs can alter the gastrointestinal microbiome and reduce gastric acid secretion, creating an environment conducive to *C. difficile* proliferation (27). Corticosteroids, by modulating the immune response, might impair the body's ability to combat infections, potentially facilitating CDI development. Therefore, the concomitant use of these medications in COVID-19 patients should be carefully considered, weighing the benefits against the potential risks. Comparable findings were reported in a recent study from Kovačević *et al.* (28) at the University Clinical Center of Vojvodina, Serbia, which analysed 5124 hospitalised COVID-19 patients and identified CDI in 6.36 % of cases. Similar to our results, the majority of affected patients were elderly (88.6 % over 65 years) and had been exposed to broad-spectrum antibiotics, most frequently quinolones, cephalosporins, and carbapenems. The Serbian study also confirmed that previous hospitalisation and antibiotic administration during hospital stay were independent risk factors for CDI development, while hypoalbuminemia emerged as a strong predictor of infection (OR = 4.15; 95 % CI: 2.37–6.41; $p = 0.019$) (28). These findings align closely with our observations in the cohort from Bosnia and Herzegovina, reinforcing the notion that excessive and often empirical antibiotic use during the COVID-19 pandemic significantly contributed to CDI incidence in elderly and high-risk patients. Both studies underline the need for stricter antimicrobial stewardship and early recognition of gastrointestinal symptoms in COVID-19 patients to prevent delayed CDI diagnosis and complications.

This study has several limitations that should be considered when interpreting the results. First, the research was conducted at a single centre, the University Clinical Hospital Mostar, which may limit the generalizability of the findings to other institutions or regions with different patient demographics, clinical practices, or resource availability. Second, the study design was retrospective and observational in nature, relying on electronic health records and aggregated data. As a result, there may be residual confounding factors that were not fully accounted for, including differences in clinical decision-making, antibiotic prescribing behaviour, or infection control measures over time.

CONCLUSIONS

The COVID-19 pandemic has profoundly reshaped healthcare systems worldwide, not only through its direct virological burden but also by amplifying the risks associated with secondary infections such as *C. difficile*. This study demonstrated a clear temporal and sta-

tistical association between the rise in COVID-19 cases and the incidence of CDI, with strong evidence linking CDI to antibiotic use, advanced age, and the administration of proton pump inhibitors and corticosteroids. While some variables such as the presence of comorbidities, did not show a statistically significant correlation with CDI in this cohort, the overall findings highlight the delicate balance between necessary COVID-19 treatments and their unintended consequences. The data reinforce the need for rigorous antimicrobial stewardship, careful risk assessment in elderly patients, and cautious use of medications that disrupt gut homeostasis during infectious disease outbreaks. In the opinion of the authors, several practical recommendations emerge to mitigate the risk of CDI during and after large-scale infectious disease outbreaks. First, hospitals should strengthen antimicrobial stewardship programs by enforcing diagnostic confirmation before initiating antibiotic therapy and by limiting the empirical use of broad-spectrum antibiotics such as cephalosporins and fluoroquinolones. Second, electronic prescribing systems should be adapted to include automatic alerts when multiple high-risk medications are prescribed concurrently. Third, periodic education and audit-feedback initiatives for clinicians and pharmacists can promote rational antibiotic use and adherence to evidence-based guidelines. The development of institution-specific protocols for de-escalation therapy and early discontinuation of antibiotics may substantially reduce unnecessary exposure, thereby decreasing CDI incidence. Implementing these targeted interventions will help preserve antibiotic efficacy, safeguard patient safety, and enhance preparedness for future pandemics.

The pandemic did not merely bring a novel viral threat but exposed systemic vulnerabilities that facilitated the resurgence of known healthcare-associated infections. Addressing these risks through proactive policy, interdisciplinary collaboration, and continued research will be essential to safeguarding patient safety in both current and future public health emergencies. These results, derived from a representative hospital in Southeastern Europe, extend the global understanding of CDI dynamics during the COVID-19 era by providing region-specific data from a healthcare system with different antimicrobial use patterns, resource constraints, and infection control infrastructure.

Institutional review board statement. – The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the University Clinical Hospital Mostar (Approval number: 208/24, dated October 17, 2024).

Informed consent statement. – Patient consent was waived due to the retrospective nature of the study, which involved only the analysis of anonymised, aggregated clinical data. No identifiable personal information was accessed, and the Ethics Committee of the University Clinical Hospital Mostar approved the use of such data without requiring individual informed consent.

Abbreviations. – CDI – *Clostridioides difficile* infection, COVID-19 – coronavirus disease 2019, SARS-CoV-2 – severe acute respiratory syndrome coronavirus 2, PCR – polymerase chain reaction, PPI – proton pump inhibitor.

Data availability statement. – Data available from authors upon request.

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Conflicts of interest. – The authors declare no conflicts of interest.

Authors contributions. – Conceptualisation, I.B. and M.K.; methodology, M.K.; validation, I.B.; formal analysis, I.E.H.; investigation, I.E.H., I.T., and I.Z.; data curation, I.I. and I.Z.; visualisation, I.Z.; supervision, I.B.; writing, original draft preparation, I.I.; writing, review and editing, M.K.; project administration, I.E.H.; funding acquisition, M.K. All authors have read and agreed to the published version of the manuscript.

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