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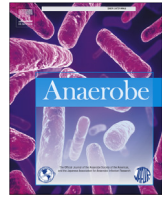
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Clostridioides difficile (including epidemiology)

Did *Clostridioides difficile* testing and infection rates change during the COVID-19 pandemic?

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ABSTRACT

Testing for and incidence of *Clostridioides difficile* infection (CDI) was examined at a single center before and during the first surge of the COVID-19 pandemic. Incidence of CDI remained stable but testing statistically significantly decreased during the first surge despite an increase in antibiotic use. There were no new CDI-focused antimicrobial stewardship interventions introduced during this time.

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While routine infection prevention practices are a priority for all healthcare systems, the COVID-19 pandemic has underscored the importance of ongoing infection prevention efforts [1]. Despite this, there has been little research on the impact of the COVID-19 pandemic on health care associated-infections (HAI) in the United States [2,3].

Current literature suggests that increased adherence to infection prevention recommendations, increased antibiotic use, improved hand hygiene, and correct donning and doffing of personal protective equipment, may have influenced HAIs in the US during the pandemic [4,5]. The aim of this study was to investigate *Clostridioides difficile* (CDI) testing and incidence during the initial surge of the pandemic. We hypothesized that strict adherence to contact precautions may have resulted in a decreased incidence of CDI in hospitalized patients during the first peak of the COVID-19 pandemic, and that CDI testing may have increased even in the absence of directed diagnostic stewardship efforts.

We conducted a single center, retrospective, observational study at the Veterans Affairs (VA) Hospital in Ann Arbor, Michigan between January 2019 and June 2020. The VA Ann Arbor is classified

as level 1a, providing the most complex level of patient care. We compared data on CDI tests from January 2019 through February 2020 to data from March 2020 (the admission of the first patient with COVID-19 at our institution) through June 2020. Pre-peak and peak periods were defined by confirmed cases in Washtenaw County [6]. No novel diagnostic or CDI-focused stewardship interventions were introduced by the antimicrobial stewardship program during the study period. Guidance on optimizing antibiotic use for secondary bacterial pneumonia was added to the institutional COVID treatment guidelines on March 30, 2020. High risk for CDI antimicrobials were not included in this guidance.

CDI testing at our institution is performed with enzyme immunoassay (EIA). A positive CDI test was defined by both glutamate dehydrogenase (GDH) and toxin. Interrupted time series analysis was performed using STATA v.16.1 software (StataCorp LLC, College Station, TX). This project received Institutional Review Board approval (IRB-2020-1234) from the Ann Arbor VA Human Studies Committee.

There were 6525 total admissions and 34,533 bed days between January 1, 2019 and June 30, 2020. The number of admissions COVID-19 ranged from 6 to 27 patients each month. The percentage of COVID-19 patients relative to total patients admitted each month was 5%, 9%, 2%, and 2% in the months March–June 2020. There were 900 total EIA tests obtained and 104 total positive cases of CDI

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between January 2019 and June 2020. Percent positivity of CDI tests ranged from 6% to 22% and was not significantly different in the pre vs. peak-pandemic periods ($p = 0.4$). Only one of those positive tests was from a patient with COVID-19. Average monthly bed days in the pre-pandemic and peak-pandemic period were not statistically significantly different (pre: 1935 days/month, peak: 1859 days/month, $p = 0.2$). There was a significant decrease in EIA tests after March 1, 2020 (the COVID peak in our region), compared to January 1, 2019–March 1, 2020. (Fig. 1). After March 1, 2020 the number of EIA tests obtained decreased by 10.2 tests each month (95% Confidence Interval [CI] -18.7 to -1.7 ; $p = 0.02$). There was no statistically significant change in the incidence of CDI/10,000 patient days ($p = 0.5$). Use of antibiotics that were defined as high risk for CDI (clindamycin, cefotaxime, ceftriaxone, ceftazidime, cefepime, cefdinir, cefpodoxime, cefixime, ciprofloxacin, gemifloxacin, levofloxacin and moxifloxacin) increased in the months of April 2020 (odds ratio = 1.4) (Fig. 2).

This retrospective, observational study examined CDI testing and diagnosis incidence before and during the first peak of the COVID-19 pandemic in Washtenaw County, Michigan. We found that while the number of admitted patients remained relatively stable, testing of CDI decreased during the first peak of the pandemic as compared to months before the initial peak. Incidence remained stable. During the first peak in our institution, elective surgeries were delayed, and some medical care transitioned from inpatient to outpatient management [7]. In addition, patients were transitioned from double occupancy to single-bed rooms and the correct donning and doffing of PPE was reinforced among hospital employees through ongoing infection prevention training. Some of these changes may have contributed to decreased testing of CDI. Incidence of CDI may have remained stable despite decreased testing due to potential over-testing or inappropriate testing before the pandemic or more thoughtful testing during the first surge. It will be interesting to monitor these trends in the future.

Our findings differ from the limited existing literature that describe increases in nosocomial infections, particularly central line-associated blood stream infection and ventilator-associated pneumonia, during the peak of the COVID-19 pandemic [8]. Other recent work has shown fewer cases of CDI despite increased

antibiotic use during their initial surge of COVID-19 patients, though large-scale studies on HAI are pending [2]. National trends in CDI have been declining in the US in recent years. However reporting during the COVID-19 pandemic may have been affected due to unexpected US Health and Human Services policies and exemptions to public reporting for HAIs afforded by the Centers for Medicare and Medicaid Services [9]. Therefore, studies at the institutional level, such as ours, may serve as snapshots into larger national CDI trends during this time.

Prior studies have found that in the treatment of COVID-19 patients, antibiotics were frequently overused in the early part of the pandemic [5,10]. At our institution, we found an increase in the use of antimicrobials overall and in high-risk CDI antibiotics between April and June 2020. While the decrease in CDI during this time occurred despite concomitant overuse of antibiotics, we were unable to determine whether there was a difference in CDI testing and antibiotic use among patients with COVID-19 patients compared to patients without COVID-19 due to limited sample size.

Our study has several limitations. First, as an observational study we are unable to establish causation. Second, institution-specific biases may have inadvertently affected the results in this single center study, limiting its generalizability. In order to preserve PPE at our institution, on March 20, 2020, patients identified to have Vancomycin-Resistant Enterococci (VRE) or Methicillin-resistant *Staphylococcus Aureus* (MRSA) infection or colonization were no longer required to use contact precautions. Although we attempted to identify concurrent changes made to CDI testing over the time period of the study that could have affected the results, it is possible that we were unable to account for all potential developments. Finally, our VA hospital has comparatively low rates of CDI at baseline with more than 30 years of fluoroquinolone restriction in place and a longstanding antimicrobial stewardship program.

In this single center study, we observed a stable incidence of CDI and decreased testing during the first peak of the COVID-19 pandemic. Understanding local HAI reporting is critical, as changes in HAI reporting structures and exemptions during this time may have affected national reporting. Further research should be undertaken to investigate the effect of COVID-19 on other HAI

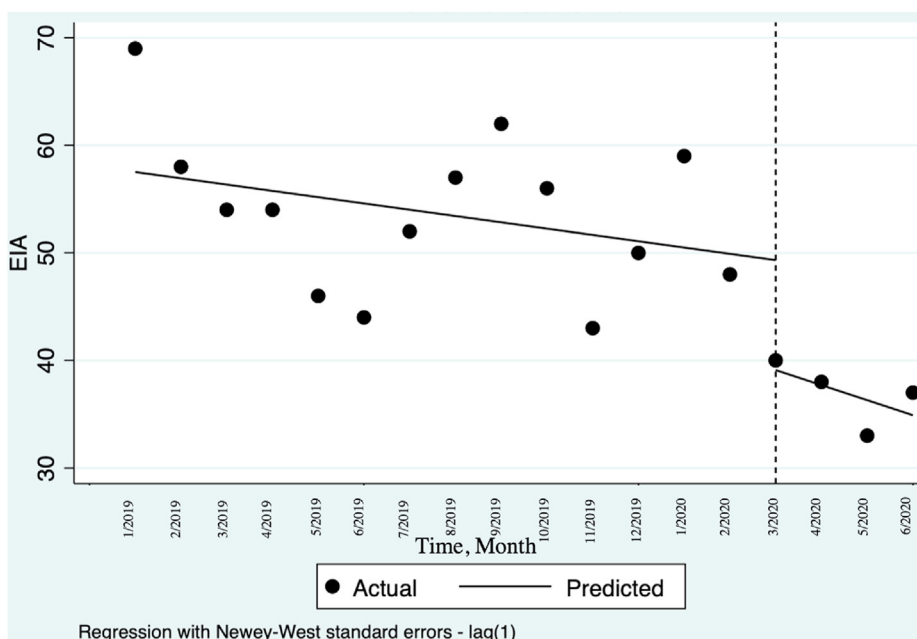


Fig. 1. Impact on incidence of EIA tests obtained for CDI

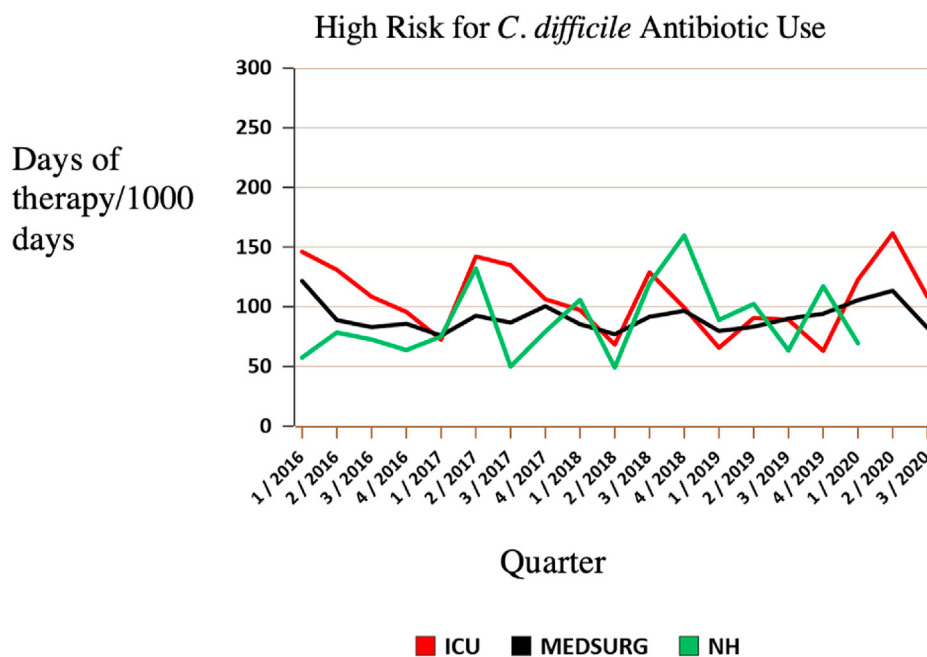


Fig. 2. High risk for CDI antibiotic use. ICU: intensive care unit. Medsurg: medical and surgical floors. NH: nursing home.

reporting within the US health care system.

Declaration of competing interest

The authors do not report any conflicts of interest.

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