Clostridium difficile: The new epidemic

J Reed, III, B Edris, S Eid, A Molitoris

Citation

J Reed, III, B Edris, S Eid, A Molitoris. *Clostridium difficile: The new epidemic*. The Internet Journal of Infectious Diseases. 2008 Volume 7 Number 1.

Abstract

Introduction: Currently Clostridium difficile associated disease (CDAD) is the most common cause of infectious diarrhea in hospitals and long-term care homes in the United States. We report prevalence of CDAD among selected DRG's and its impact on mortality rates, mean length of stay (LOS), and total patient costs at a large community, teaching hospital.
Methods: Data were abstracted using the hospital's administrative data warehouse. 9,164 patients with a hospital admission between 01/01/2002 and 12/31/2006, assigned a DRG of Heart Failure & Shock, major small and large bowel procedures, Esophagitis both with and without complications and comorbidities, OR procedures for infectious diseases, and Septicemia were included.
Results: LOS for patients with CDAD was more than double that for patients without CDAD (13.5 ± 14.9 days versus 5.4 ± 5.6 days, p = 0.001). Average charges for patients with CDAD was tripled ($24,854 ± $41,095 versus $7,704 ± $11,061, p = 0.001). The hospital length of stay doubled in four of the five DRGs. The patient cost also doubled in the same DRGs.
Conclusion: Patients with CDAD typically have mean LOS and average costs double that of patients without CDAD.

INTRODUCTION

From 1995 to 2005, the number of Pennsylvania hospitalizations for Clostridium difficile-associated disease (CDAD) increased from 7,026 to 20,941. This represents an amazing 173% increase, from 4.4 cases per 1,000 hospitalizations to 12.0 per 1,000 hospitalizations. Patients with CDAD were hospitalized over twice as long, charged more than twice as much, and were four times as likely to die as patients without CDAD. [16]

Antibiotic-associated diarrhea and colitis became well established soon after antibiotics were first made available. By 1978, Clostridium difficile became the prevalent pathogen in the majority of cases where antibiotics were related to such intestinal distress. [2] The most prescribed antibiotic was clindamycin and the standard management was to withdraw the implicated antibiotic and begin treating with vancomycin. From 1983 through 2003, the most commonly implicated antibiotics were cephalosporins and metronidazole replaced vancomycin as the standard treatment while principles of containment became infection control and antibiotic control. From 2003 to 2006, Clostridium difficile (NAP1, BI, or 027) emerged as the most virulent and common cause of infectious diarrhea in hospitals and long-term care homes in the United States, Japan and Europe. [2,4,5,8,9] This particular strain of CDAD is more frequent, severe, resistant to standard therapy, and likely to relapse than any other present strain and it is believed that the high resistance of this strain reflects the overuse of cephalosporins and fluoroquinolones within the past several years. Although the bacterium that is responsible for CDAD has been around since 1978, these recent more virulent strains have resulted in a new interest in this “old pathogen.” [18]

Successful management of CDAD requires early detection of infections, rapid treatment, and strict implementation of infection control policies and procedures. [3,17] According to the Society for Healthcare Epidemiology of America standard recommendations for infection control in CDAD infected patients include patient isolation in a single room, contact precautions, and the use of special bleach cleansers for cleaning purposes. The most important method of prevention, however, is hand washing using soap and water since alcohol-based sanitizers are unable to kill clostridia spores. [2] As this new CDAD epidemic grows it is important for researchers and practitioners to be aware of and understand the impact of CDAD within their healthcare settings.

The objective of this study was to report the prevalence of

Clostridium difficile associated disease among selected Diagnosis Related Groups and examine the impact this bacterium has on mortality rates, mean length of stay (LOS), and total patient costs at a large academic, community hospital.

METHODS

Data for this study were abstracted using the hospital's private administrative data warehouse. 9,164 patients with a hospital admission between 01/01/2002 and 12/31/2006, who were assigned a DRG of 127 (heart failure & shock), 148 (major small and large bowel procedures with complications and comorbidities), 182 (esophagitis, gastroenteritis, and miscellaneous digestive disorders age >17 with complications and comorbidities), 415 (operating room procedures for infectious and parasitic diseases), and 416 (septicemia age >17) were included.

RESULTS

The hospital length of stay for patients with CDAD was more than double that of patients without CDAD (13.5 ± 14.9 days versus 5.4 ± 5.6 days, p = 0.001). The average charges for patients with CDAD was tripled ($24,854 ± $41,095 versus $7,704 ± $11,061, p = 0.001) when compared to those not infected. Overall the hospital length of stay doubled in four of the five DRG groups and patient costs also doubled in the same DRGs, as well (Table 1).

Figure 1

Table 1: LOS/Total Cost/Mortality of CDAD in Selected DRGs (1/1/2002-12/31/2006)

	n	LOS	Charges
DRG 127: Congestive Heart Failure			
w/ CDAD	35	9.7 ± 7.0	$12,487 ± $11,727
w/o CDAD	2507	5.2 ± 3.9	$6,275 ± $5,542
p-value		0.001	0.001
DRG 148: Major small & large bowel procedures w cc			
w/ CDAD	45	20.9 ± 11.3	$39,875 ± $26,521
w/o CDAD	990	9.9 ± 7.0	$18,290 ± $15,389
p-value		0.001	0.001
DRG 182: Esophagitis, gastroent & misc digestive disorders w cc			
w/ CDAD	320	6.9 ± 5.2	$7,690 ± 6,836
w/o CDAD	2074	3.8 ± 3.5	$4,581 ± 4,024
p-value		0.001	0.001
DRG 415: OR procedure for infectious & parasitic diseases			
w/ CDAD	32	14.7 ± 8.6	$30.098 ± $21,603
w/o CDAD	417	12.5 ± 10.0	$23,760 ± $24,863
p-value		0.00	0.001
DRG 416: Septicemia (age > 17)			
w/ CDAD	92	10.7 ± 7.6	$18,960 ± $17,446
w/o CDAD	1119	6.4 ± 5.2	$11,215 ± $11,492
p-value		0.001	0.001

DISCUSSION

Clostridium difficile is an anaerobic, spore-forming bacillus that is responsible for a spectrum of CDAD, including uncomplicated diarrhea, pseudomembranous colitis, and toxic megacolon. Infections caused by CDAD are a growing public health concern. United States hospital discharges for which CDAD was listed as one of the discharge diagnoses doubled from 31/100,000 in 1996 to 61/100,000 in 2003. The overall rate during this period was higher in hospitalized persons aged 65 and older and prevalence is increasing in residents of long-term-care facilities. Accompanying this increasing rate of CDAD are increased morbidity and mortality rates, increased risk of relapse and more disease associated complications. This is in large part due to a new epidemic strain, termed ribotype 027 that has emerged over the past several years disproportionately affecting older persons. [4,7,9]

CDAD is a common and serious infectious complication associated with a substantial morbidity and mortality and hospital infection control specialists report an increasing poor response to metronidazole treatment. [10] Also, the financial burden of CDAD on healthcare facilities is increasing as the incidence of CDAD continues to rise. [7,11] Archibald and colleagues reported results of their study from the National Nosocomial Infections Surveillance System 1987 - 2001 (NNISS) on CDAD in medicine, surgery, obstetrics and gynecology, pediatrics, and neonatal medicine services. [1] Hospital-wide CDAD rates increased in hospitals with fewer than 250 beds and were significantly higher in teaching versus non-teaching hospitals (13.0 versus 11.7 cases per 10,000 hospitalizations). Medical services had 18.9 cases, followed by surgical (15.6 cases), gynecology (6.0), pediatrics (2.8), obstetrics (1.0) and neonatal (0.5 cases).

In Pennsylvania the alarming impact of CDAD in healthcare facilities can be readily seen. In a report disseminated by the Pennsylvania Health Care Cost Containment Council (PHC4), [16] the number of Pennsylvania hospitalizations for CDAD increased form 7,026 in 1995 to 20,941 in 2005, an increase from 4.4 cases per 1,000 hospitalizations to 12.0 per 1,000 hospitalizations. In addition, patients with CDAD were hospitalized two and a half times longer (4.7 days versus 11.4 days), charged more than twice as much ($30,833 versus $73,576), and were four times more likely to die as patients without CDAD (2.1% versus 8.7%). The older population (specifically patients aged 65 years and older) seems to be experiencing the brunt of this epidemic. In 1995, this age group had the highest rate of CDAD with 7.1 cases per 1,000 hospitalizations. This number only increased and in 2005 there were 19.3 cases per 1,000

hospitalizations. Alarmingly, this high rate of CDAD hospitalizations for patients aged 65 and older in Pennsylvania mirrors national reports on CDAD hospitalization rates. [10]

There is a seasonal variation in CDAD occurrence in ICUs with higher rates occurring during winter months versus non-winter months. Increased patient census, potential lower nurse-to-patient ratios, greater severity of illness, and the tendency of hospitals to admit higher numbers of patients with respiratory infections during the winter months contribute to a parallel increase in antimicrobial use and a resultant surge in CDAD rates. [1] The severity of this bacterium has never been underestimated, but the infection was viewed as primarily a problem for healthcare facilities rather than an issue within the community setting. More recently, however, CDAD has been reported frequently in non-hospital-based settings. Therefore, research efforts focused on CDAD began to shift to include emerging strains that have surfaced within the community, widening the impact of this epidemic. Initial reports indicate that these community strains afflict mainly children and young healthy women, populations once considered low risk, which demonstrates the severity of this epidemic. [3,14]

For the several years after Clostridium difficile was recognized as a cause of antibiotic-associated diarrhea, oral vancomycin was considered to be the treatment of choice. In the early 1980s studies suggested that oral metronidazole was therapeutically equivalent. However, the failure rate of metronidazole (16%-38%) treatment of CDAD has been increasing. [12,15] After nearly 30 years of dealing with CDAD, the treatment options are essentially limited to two medications (vancomycin and metronidazole). Emerging therapies include rifaximin, nitazoxanide, intravenous immunoglobulin, and finidazole. These treatment options have been shown to be successful when other agents have either failed or were contraindicated, although additional studies are needed. [6,13]

Prevention strategies include contact precautions for all patients with known CDAD, patient placement in a private room, and patient cohorting (patients with CDAD sharing the same room, provided each is transferred out of the room once diarrhea ceases) and have been shown to be effective. Compounding the prevention of CDAD is the resistance of Clostridium difficile spores to eradication. Clostridium difficile spores have the ability to survive on dry surfaces for several months and are not killed by alcohol cleansing.

There has been some concern that the widespread use of alcohol-based hand sanitizers for health care workers may have had a role in the increased CDAD rates. Unfortunately, with the spread of NAP1/BI/027 Clostridium difficile to half of the states in the United States, most of Canada, and Western Europe, it is more likely that rates of CDAD will continue to increase. [3]

CORRESPONDENCE TO

James F. Reed, III Lehigh Valley Hospital & Health Network 6T28, Health Studies 17 [[[th]]] and Chew Streets, P.O. Box 7017 Allentown, PA 18105-7017 Phone: 610-969-4785, Fax: 610-969-2247 James_F.Reed@lvh.com

References

1. Archibald, L.K., Banerjee, S.N., and W.R. Jarvis. 2004. Secular trends in hospital-acquired Clostridium difficile disease in the United States, 1987-2001. J. Inf. Dis. 189:1585-1589.
2. Bartlett, J. 2006. Narrative Review: The New Epidemic of Clostridium difficile-Associated Enteric Disease. Ann. Int. Med. 145(10): 758-764.
3. Blossom, D.B., and L.C. McDonald. 2007. The challenges posed by reemerging Clostridium difficile infection. Clin. Inf. Dis. 45:222-227.
4. Centers for Disease Control and Prevention. 2005. Severe Clostridium difficile-associated disease in populations previously at low risk - four states, 2005. MMWR. 54(47):1201-1205.
5. Cloud, J., and C.P. Kelly. 2007. Update on Clostridium difficile associated disease. Curr. Opin. Gastroenterol. 23(1):4-9.
6. Jodlowski, T.Z., Oehler, R., Kam, L.W., and I. Melnychuk. 2006. Emerging therapies in the treatment of Clostridium difficile - associated disease. Ann. Pharmacotherapy. 40:2164-2169.
7. Kuijper, E.J., Coignard, B., and P. Tull. 2006. ESCMID Study Group for clostridium difficile: EU member states; European Centre for Disease Prevention and Control. Emergence of clostridium difficile-associated disease in North America and Europe. Clin. Microbiol. Inf. 12(Suppl 6):2-18.
8. Kuijper, E.J., van Dissel, J.T., and M.H. Wilcox. 2007. Clostridium difficile: changing epidemiology and new treatment options. Curr. Opin. Infect. Dis. 20(4):376-383.
9. McDonald, L.C., Owings, M., and D.B. Jernigan. 2006. Clostridium difficile infection in patients discharged from US short-stay hospitals, 1996-2003. Emerg. Infect. Dis . 12(3):409-415.
10. McFarland, L.V., Beneda, H.W., Clarridge, J.E., and G.J. Raugi. 2007. Implications of the changing face of Clostridium difficile disease for health care practitioners. Am. J. Infect. Cont. 35(4):237-253.
11. Miller, M.A., Hyland, M., Ofner-Agostini, M., Gourdeau, M., and M. Ishak. 2002. Canadian Hospital Epidemiology Committee. Canadian Nosocomial Infection Surveillance Program. Morbidity, mortality, and healthcare burden of nosocomial Clostridium difficile-associated diarrhea in Canadian hospitals. Inf. Cont. Hosp. Epidemiol. 23(3):137-140.
12. Musher, D.M., Aslam, S., Logan, N., Nallacheru, S., Bhaila, I., Borchert, F., and R.J. Hamill. 2005. Relatively

poor outcome after treatment of Clostridium difficile colitis with metronidazole. Clin. Inf. Dis. 40:1586-1590.
13. Musher, D.M., Logan, N., and V. Mehendiratta, et al. 2007. Clostridium difficile colitis that fails conventional metronidazole therapy: response to nitazoxanide. J. Antimicrobial Chemotherapy. 59:705-710.
14. Oldfield, E.C. 2006. Clostridium difficile-associated diarrhea: resurgence with a vengeance. Rev. Gastroenterol. Disord. 6(2):79-96.
15. Pepin, J., Alary, M.E., and L. Valiquette, et al. 2005. Increasing risk of relapse after treatment of Clostridium difficile colitis in Quebec, Canada. Clin. Inf. Dis. 40:1591-1597.
16. PHC4 Research Brief. Clostridium difficile Infections in Pennsylvania Hospitals, Issue No. 11, May 2007.
17. Price, M., Dao-Tran, T., and K. Garey, et al. 2007. Epidemiology and incidence of Clostridium difficile-associated diarrhea diagnosed upon admission to a university hospital. J. Hosp. Inf. 65: 42-46.
18. Stone, S., Beric, V., and A. Quick, et al. 1998. The effect of an enhanced infection-control policy on the incidence of Clostridium difficile infection and methicillin-resistant Staphylococcus aureus colonization in acute elderly medical patients. Age and Ageing. 27: 561-568.

Author Information

James F. Reed, III
Health Studies Department, Lehigh Valley Hospital

Bree A. Edris
Health Studies Department, Lehigh Valley Hospital

Sherrine Eid
Health Studies Department, Lehigh Valley Hospital

Allison Molitoris
Health Studies Department, Lehigh Valley Hospital