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Economic burden of primary compared with recurrent *Clostridium difficile* infection in hospitalized patients: a prospective cohort study☆

D.N. Shah [a], S.L. Aitken [a,b], L.F. Barragan [c], S. Bozorgui [c], S. Goddu [c], M.E. Navarro [c], Y. Xie [d], H.L. DuPont [a,c,e,f], K.W. Garey [a,f,*]

[a] *Department of Pharmacy Practice and Translational Research, University of Houston College of Pharmacy, Houston, TX, USA*
[b] *Division of Pharmacy, The University of Texas MD Anderson Cancer Center, Houston, TX, USA*
[c] *Internal Medicine Service, Baylor St Luke's Medical Center, Houston, TX, USA*
[d] *Department of Outcomes Research, Merck & Co., Whitehouse Station, NJ, USA*
[e] *Division of Infectious Diseases, Baylor College of Medicine, Houston, TX, USA*
[f] *Center for Infectious Diseases, University of Texas School of Public Health, Houston, TX, USA*

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SUMMARY

Background: Few studies have investigated the additional healthcare costs of recurrent *C. difficile* infection (CDI).
Aim: To quantify inpatient treatment costs for CDI and length of stay among hospitalized patients with primary CDI only, compared with CDI patients who experienced recurrent CDI.
Methods: This was a prospective, observational cohort study of hospitalized adult patients with primary CDI followed for three months to assess for recurrent CDI episodes. Total and CDI-attributable hospital length of stay (LOS) and hospitalization costs were compared among patients who did or did not experience at least one recurrent CDI episode.
Findings: In all, 540 hospitalized patients aged 62 ± 17 years (42% males) with primary CDI were enrolled, of whom 95 patients (18%) experienced 101 recurrent CDI episodes. CDI-attributable median (interquartile range) LOS and costs (in US$) increased from 7 (4–13) days and $13,168 (7,525–24,456) for patients with primary CDI only versus 15 (8–25) days and $28,218 (15,050–47,030) for patients with recurrent CDI ($P < 0.0001$, each). Total hospital median LOS and costs increased from 11 (6–22) days and $20,693 (11,287–41,386) for patients with primary CDI only versus 24 (11–48) days and $45,148 (20,693–82,772) for patients with recurrent CDI ($P < 0.0001$, each). The median cost of pharmacological treatment while hospitalized was $60 (23–200) for patients with primary CDI only ($N = 445$) and $140 (30–260) for patients with recurrent CDI ($P = 0.0013$).

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* Corresponding author. Address: University of Houston College of Pharmacy, Houston, TX 77030, USA. Tel.: +1 832 842 8386; fax: +1 713 795 8383.
E-mail address: kgarey@uh.edu (K.W. Garey).

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Conclusion: This study demonstrated that patients with CDI experience a significant healthcare economic burden attributed to CDI. Economic costs and healthcare burden increased significantly for patients with recurrent CDI.

Introduction

Clostridium difficile infection (CDI) is the most frequent cause of infectious diarrhoea in hospitalized patients in the USA and is the most prevalent healthcare-associated pathogen.[1] The US Centers for Disease Control and Prevention (CDC) estimate that there are ~250,000 cases of CDI per year, 14,000 deaths, and more than US$1 billion in healthcare costs associated with CDI.[2] One of the most feared but widespread complications is recurrence, which occurs in 25–33% of patients with primary CDI treated with metronidazole or oral vancomycin.[3,4] In addition to increased mortality and morbidity, recurrent CDI is also associated with increased healthcare costs.[5,6] Recurrent CDI leads to significant health resource utilization including frequent re-hospitalizations.[7] However, few studies have investigated the economic costs of recurrent CDI compared with primary CDI.[5] The objective of this study was to quantify inpatient treatment costs for CDI and length of stay (LOS) among hospitalized patients with primary CDI only, compared with CDI patients who experienced recurrent CDI.

Methods

This was a prospective single-centre, observational cohort study of hospitalized adult patients at a large, university-affiliated, tertiary care hospital in Houston, Texas. All adult (≥18 years) patients with a diagnosis of CDI were eligible for inclusion. Exclusion criteria included discharge prior to reporting of *C. difficile* test result or unable to obtain informed consent. CDI was defined as diarrhoea plus positive diagnostic test for *C. difficile* toxin. The assays used were the *C. difficile* cytotoxicity assay (2007–2010) and the BD GeneOhm™ Cdiff, real-time polymerase chain reaction (PCR) assay for toxin B gene (2010–2013). The decision to test for CDI was made by the patient's primary medical or infectious diseases (ID) consulting team. Patients were classified as having primary CDI if this was their first episode of CDI. Primary CDI was assessed by a thorough medical chart review as well as by direct patient interview to assess for any prior occurrence of CDI. Another CDI episode(s) within three months following completion of antibiotic treatment for primary CDI was considered a recurrent CDI episode. Patients were considered to have recurrent CDI based on presence of diarrhoea, a positive diagnostic test for *C. difficile*, and receipt of anti-*C. difficile* antibiotics. Hospital admission attributed to CDI was defined as CDI diagnosis within 72 h of admission. The treatment of CDI and the selection of antibiotic to treat CDI were made by the patient's primary medical or ID consult team. Since May 2010, as part of a hospital-wide antimicrobial stewardship protocol, the majority of patients with severe CDI (as defined using a modified severity scale proposed by Zar *et al.*[8]) were treated with oral vancomycin.

Data were prospectively obtained from patient's online medical chart and/or by direct patient interview. Data collected included age, gender, admission date, discharge date, collection date of stool for diagnostic test, CDI treatment-related data including name of antimicrobials, dose, route, and frequency, start and stop date of treatment; along with clinical parameters. The severity of underlying illness was based on the Horn Index.[9] The study was approved by the institutional review boards of Baylor St Luke's Medical Center and the University of Houston.

Data analyses

The total hospital LOS was calculated for each patient. The number of days in hospital from the date of CDI diagnosis was evaluated for CDI-attributable LOS. Total and CDI-attributable hospitalization costs (US$) were estimated based on Healthcare Cost and Utilization Project data (http://www.hcup-us.ahrq.gov/reports/statbriefs/sb124.pdf) for average daily healthcare costs multiplied by the total and CDI-attributable length of hospital stay, respectively. All pharmacological treatment that patients received for CDI were included in the CDI pharmacological treatment costs including one-time doses. For patients who received multiple medications for CDI during the stay, the cost for each medication was included and then summed for a total pharmacological cost. CDI pharmacological treatment costs were based on average wholesale drug price (online.lexi.com, Red Book Online, Truven Health Analytics, Micromedex Solutions, Michigan, USA). At the study institution, instead of the commercially available oral vancomycin, a compounded formulation of oral vancomycin was used, and thus the price used for this was the per-hospital price.

Total hospital LOS, CDI-attributable LOS, and pharmacological and hospitalization costs were compared between patients with primary CDI only versus patients who experienced recurrent CDI. Results are expressed as medians [interquartile range (IQR)] and evaluated using non-parametric statistics. $P < 0.05$ was considered significant.

Results

In all, 540 hospitalized patients with a median age of 62 ± 17 years (42% males) with primary CDI between 2007 and 2013 met the inclusion criteria for the study. Ninety-five of 540 patients (18%) experienced 101 episodes of recurrent CDI, of which 89 patients had one recurrence and six patients had more than one recurrence. CDI-attributable admissions occurred in 307 out of 540 (57%) primary CDI episodes and 64 out of 101 (63%) recurrent CDI episodes. Baseline characteristics of patients stratified by those with primary CDI only compared to patients who also experienced recurrent CDI episodes are shown in Table I. Of patients with recurrent CDI ($N = 95$), 64% ($N = 61$) had an attributable admission due to CDI for the primary episode and 40% ($N = 38$) for the secondary episode. For 18 patients, the recurrent episode occurred during the same hospitalization as the primary episode. For patients with primary CDI only, the CDI-attributable median LOS was 7 (IQR: 4–13) days versus 15 (IQR: 8–25) days for patients with recurrent CDI ($P < 0.0001$).