Racial Differences in *Clostridium difficile* Infection Rates Are Attributable to Disparities in Health Care Access

Eric J. Mao, Colleen R. Kelly, Jason T. Machan

The Warren Alpert Medical School of Brown University, Providence, Rhode Island, USA; Division of Gastroenterology, Rhode Island Hospital, Providence, Rhode Island, USA; Lifespan Hospital System, Providence, Rhode Island, USA; Departments of Orthopedics and Surgery, Rhode Island Hospital, Providence, Rhode Island, USA

This study confirms previously reported racial differences in *Clostridium difficile* infection (CDI) rates in the United States and explores the nature of those differences. We conducted a retrospective study using the 2010 Nationwide Inpatient Sample, the largest all-payer database of hospital discharges in the United States. We identified hospital stays most likely to include antibiotic treatment for infections, based on hospital discharge diagnoses, and we examined how CDI rates varied, in an attempt to distinguish between genotypic and environmental racial differences. Logistic regressions for the survey design were used to test hypotheses. Among patients likely to have received antibiotics, white patients had higher CDI rates than black, Hispanic, Asian, and Native American patients (*P* < 0.0001). CDI rates increased with higher income levels and were higher for hospitalizations paid by private insurance versus those paid by Medicaid or classified as self-pay or free care (*P* < 0.0001). Among patients admitted from skilled nursing facilities, where racial bias in health care access is less, racial differences in CDI rates disappeared (*P* = 1.0). Infected patients did not show racial differences in rates of complicated CDI or death (*P* = 1.0). Although white patients had greater CDI rates than nonwhite patients, racial differences in CDI rates disappeared in a population for which health care access was presumed to be less racially biased. This provides evidence that apparent racial differences in CDI risks may represent health care access disparities, rather than genotypic differences. CDI represents a deviation from the paradigm that increased health care access is associated with less morbidity.

*Clostridium difficile* infection (CDI) has become an increasingly common and morbid condition. Hospital discharges in the United States with CDI as any listed diagnosis more than doubled from 134,361 in 2000 to 291,303 in 2005 (1). Three million incident cases of *C. difficile* are estimated to occur each year, with excess hospital costs of $2.2 billion dollars (2, 3). Recognized CDI risk factors include advanced age, exposure to antibiotics, health care environment exposure, and possibly gastric acid suppression (3–13). Although previous studies suggested racial differences in CDI risks and mortality rates (14–16), the current literature does not identify race as a risk factor for CDI. This study utilized discharge data from the Nationwide Inpatient Sample (NIS), Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality (www.hcup-us.ahrq.gov/nisoverview.jsp), to evaluate whether CDI rates vary with race, to explore confounders of the relationship between race and CDI rates, and to investigate whether racial disparities in CDI rates persist when confounders are minimized.

**MATERIALS AND METHODS**

**Study database.** We conducted a retrospective epidemiological study using the 2010 Nationwide Inpatient Sample, an all-payer database of community hospital discharges in the United States that is maintained by the Healthcare Cost and Utilization Project of the Agency for Healthcare Research and Quality. The database contained 7.8 million discharge records from 1,051 community hospitals in the United States, representing approximately 39 million nationwide hospital discharges in 2010.

**Study design.** CDI rates according to race were investigated in the entire national database in the initial analysis. Exposure to antibiotics, which is the greatest risk factor for CDI, may vary between races; therefore, our study investigated CDI rates according to race in a population likely exposed to antibiotics and thus at high risk for developing CDI. Since the database does not contain data on antibiotic therapy, bacterial infection was used as a proxy for antibiotic exposure. Hospitalizations that carried a diagnosis of bacterial infection were interpreted as instances of patient exposure to antibiotics. Patients were identified as having likely antibiotic exposure on the basis of any discharge diagnosis with an International Classification of Diseases, 9th Revision (ICD-9), code for any bacterial infection or CDI. Hospitalizations with a CDI diagnosis were included in the study sample with likely exposure to antibiotics under the assumption that the patients likely received recent antibiotic treatment as an inpatient or an outpatient, since the greatest risk factor for CDI is antibiotic exposure. Total abdominal colectomy with a diagnosis of CDI was included because this surgical procedure almost certainly represented a complication of a preceding CDI. The primary outcome was CDI, as identified by an ICD-9 code for CDI during the same hospital stay; CDI rates were compared according to racial classifications of white, black, Hispanic, Asian, or Native American, in (i) the entire database, (ii) the study sample of hospital discharges with likely antibiotic exposure (discharges with diagnoses of any bacterial infection, CDI, or CDI with a procedure code for a total abdominal colectomy), and (iii) a subpopulation of hospital discharges with likely antibiotic exposure with a point of origin at a skilled nursing facility. Race was defined by the patient’s hospital discharge record. CDI rates were also compared according to race confounders of age, sex, median annual household income, and primary payer for the hospital stay. CDI-related mortality rates were compared according to race. Complicated CDI rates, designated by an ICD-9 code...
for CDI with a diagnosis of megacolon, bowel perforation, or total abdominal colectomy, were compared according to race.

**Statistical methods.** Logistic regressions designed to take into account the survey design, according to the Healthcare Cost and Utilization Project documentation (surveylogistic procedure in SAS version 9.3; SAS Institute, Cary, NC) (17), were used for hypothesis testing regarding CDI rates. Rather than using standard multiple logistic regression in an attempt to separate statistically the effects of potential confounders from the effects of race, which we anticipated would represent higher-order interactions (race affects different multifactor subgroups differently), the methodological decision was made to test for race effects within targeted subgroups of patients. These subgroups were chosen carefully, based on theoretical reasoning, and were empirically confirmed by the sequence of our analyses, with the goal of minimizing the real-world effects of likely confounders (age, median income, and insurance type) and maximizing our power to detect differences because of known high rates. Therefore, our analyses of risks for CDI culminated in a comparison according to race of patients in skilled nursing facilities. Also, because the methods for analysis were specialized for such survey designs, relevant domains were created and integrated into models using all patient records, rather than extracting the subsets of patients of interest for each analysis, which could bias results. More specifically, records were specified as having likely antibiotic exposure for some analyses, and likely antibiotic exposure was cross-tabulated with point of origin as indicated in the analyses.

**RESULTS**

**Patients with likely antibiotic exposure and CDI.** Approximately 4.2 million patients were defined as likely being exposed to antibiotics, based on having a hospital discharge diagnosis of any bacterial infection, CDI, or CDI with total abdominal colectomy. Approximately 178,000 of these cases also included a CDI discharge diagnosis.

**CDI rates by race.**

**(i) Total NIS population.** In the entire NIS population, white patients had a higher CDI rate than black, Hispanic, Asian, and Native American patients (adjusted P values of <0.001). Black patients had a higher CDI rate than Hispanic and Asian patients but not Native American patients (adjusted P values of <0.001, 0.0032, and 0.0589, respectively), although black patients did exhibit a higher CDI rate than Native American patients (unadjusted P value of 0.0074) (Fig. 1A).

**(ii) Population with likely antibiotic exposure (high-risk population).** In the study sample of hospital discharges with likely exposure to antibiotics, white patients again demonstrated a higher CDI rate than black, Hispanic, Asian, and Native American patients (adjusted P values of <0.0001, <0.0001, 0.0342, and <0.0001, respectively). Black patients had a higher CDI rate than Native American patients (adjusted P value of 0.0024) but not Asian or Hispanic patients (adjusted P values of 0.8101 and 0.3088, respectively), although black patients did exhibit a higher CDI rate than Hispanic patients (unadjusted P value of 0.0074) (Fig. 1A).

**CDI rates and potential confounders of race effects.** CDI rates increased in older age cohorts. There were no differences in CDI rates between Asian patients and Native American patients (adjusted P value of 0.3781) (Fig. 1B).
adjusted $P$ values of 0.6413, 0.1764, and 0.1764, respectively). CDI rates increased linearly for increasing age cohorts of 30 to 39, 40 to 49, 50 to 59, 60 to 69, 70 to 79, and ≥80 years (adjusted $P$ values of <0.0001), except for comparisons of cohorts of 40 to 49 years versus 50 to 59 years and cohorts of 70 to 79 years versus ≥80 years (adjusted $P$ values of 0.1764 and 0.6413, respectively). CDI rates were not different for men versus women (adjusted $P$ value of 0.1070). CDI rates increased linearly with progressive median annual household income quartiles of less than $41,000, $41,000 to $66,999, and ≥$67,000 or more (adjusted $P$ values of <0.0001) (Fig. 2). The CDI rate was higher for hospital stays paid by private insurance versus hospital stays paid by Medicaid, classified as self-pay, or provided as free care (adjusted $P$ values of <0.0001). Hospitalizations paid by Medicare had the highest CDI rate (adjusted $P$ value of <0.0001). Hospitalizations paid by Medicaid had a higher CDI rate than hospitalizations classified as self-pay or free care (adjusted $P$ values of <0.0001 and 0.0250, respectively). Hospitalizations classified as self-pay or free care did not show any differences in CDI rates (adjusted $P$ value of 0.9813) (Fig. 3).

**CDI rates by race and age.** Since increasing age is strongly correlated with greater rates of CDI, it is possible that potential differences in age compositions of different racial groups could be driving perceived racial differences in CDI rates. In order to investigate whether age is the primary driver of CDI rates in our population, we examined CDI rates by race within different age cohorts. In the age cohorts of <20, 20 to 29, 70 to 79, and ≥80 years, white patients had significantly greater rates of CDI than black patients ($P$ values of <0.0001, 0.0023, 0.0410, and 0.0065, respectively). In the age cohorts of 20 to 29, 30 to 39, 50 to 59, and 70 to 79 years, white patients had significantly greater rates of CDI than Hispanic patients ($P$ values of 0.0002, <0.0001, 0.0071, 0.0079, and 0.0004, respectively). Within uniform age cohorts, racial differences in CDI rates persisted.

**CDI rates by race in subpopulation with minimized confounding and maximized power.** In order to elucidate the apparent racial disparity in CDI risk, we identified a subpopulation of patients with similar health care access in 166,000 hospitalizations with likely antibiotic exposure and a point of origin of a skilled nursing facility. There was less variation in health care access in this subpopulation, as these patients possessed a certain threshold of health care access in the form of income or health insurance to cover skilled nursing facility expenses. Within this subpopulation, approximately 13,900 hospitalizations included a diagnosis of CDI. In this subpopulation, there were no differences in CDI rates between races (adjusted $P$ values of 1.0000) (Fig. 1C).

**Complicated CDI rates and CDI-related mortality rates by race.** There were no differences in CDI-related mortality rates between races (adjusted $P$ values of 1.0000) (Fig. 4A). White patients did not have greater complicated CDI rates than black, Hispanic, and Asian patients (adjusted $P$ values of 1.0000). There were no differences in complicated CDI rates when black patients were compared with Hispanic and Asian patients (adjusted $P$ values of 1.0000). There were no differences in complicated CDI rates between Hispanic and Asian patients (adjusted $P$ value of 0.8239). There were not sufficient numbers of Native American patients available for complicated CDI analysis (Fig. 4B).

**DISCUSSION**

On the surface of the CDI epidemic, there appears to be an increased disease burden among white patients versus nonwhite patients, as reflected in this study by the higher CDI rate among white patients in the entire represented population of the database. This increased CDI burden among white patients persisted in the study population with likely antibiotic exposure. Based on these observations, it might be questioned whether CDI risk differences reflect intrinsic, genetically linked, immunological differences in resistance to *C. difficile* colonization and/or infection.

Given that race is commonly confounded by socioeconomic factors, we analyzed CDI risks through the lenses of income and hospital stay primary payer. As the level of health care access increased in higher income quartiles and with more comprehensive health insurance, CDI risks increased. The primary payer of Medicare carried the highest CDI risk. In addition to increased health care access, this population consists primarily of elderly patients, and age is another major risk factor for CDI. Although age was strong correlated with CDI rates, especially in the population >65 years of age, which accounts for the majority of the Medicare...
population, racial differences in CDI rates persisted within age cohorts. Elderly white patients experienced higher CDI rates than elderly black and Hispanic patients. Therefore, age is not driving racial differences in CDI rates in this population. The increased CDI risk associated with Medicare, Medicaid, and private insurance, compared with self-pay and free care, may reflect greater cumulative exposure to antibiotics in the outpatient or inpatient setting and a greater likelihood of \textit{C. difficile} exposure through increased health care setting interactions. The demonstrated effect of health care access on CDI risk supports socioeconomic status as an alternative to a genotypic effect of race on CDI risk. Hence, disproportionate CDI risk may be driven by the environmental risk factor of disparate health care access.

The apparent race effect on CDI risk disappeared in a patient population for which variations in socioeconomic status factors were lessened and rates of exposure to CDI, as well as actual rates of CDI, were high, which supplied the best opportunity to detect differences. Of the hospital discharges with likely antibiotic exposure, those with a point of origin of a skilled nursing facility reflected a population of patients of similar age, comorbidities, and access to health care. There were no differences in CDI rates between races in this analysis, suggesting that racial differences in CDI risks may be environmentally driven.

There were no racial differences in CDI-related mortality rates. Although white patients may be at greater risk than nonwhite patients for CDI, there was no apparent race effect on CDI-related mortality rates once CDI developed. CDI-related mortality rates may be driven by the overall poor condition of patients in this typically elderly population with multiple comorbidities. This is inconsistent with a previous study showing white patients to have higher CDI-related mortality rates than other racial groups (16). Methodologically different, our study investigated CDI-related mortality rates in a population with likely antibiotic exposure, which causes intestinal bacterial disruption and promotes active CDI. The previous study investigated CDI-related mortality rates utilizing mortality records for the national population. Our analysis focused on a population with likely exposure to antibiotics, removing the element of racial variations in antibiotic exposure. We think that our analysis provides a more accurate representation of CDI-related mortality rates for patients who are at risk for the disease.

With the hypothesis that racial differences in CDI rates are driven by disparities in health care access, the higher CDI rate among white patients reflects greater resources of higher income or more comprehensive health insurance, compared with other racial groups. Similar CDI rates for black, Hispanic, and Asian patients suggest similar health care access among these populations. In the United States in 2009, however, Asian individuals had a higher median annual household income than did black, white, and Hispanic individuals (http://www.census.gov/compendia/statab/2012/tables/12s0691.pdf). Unfortunately, only data on median annual household incomes based on ZIP codes, and not individual income levels, were available for analysis in the Nationwide Inpatient Sample. This suggests that other factors, including cultural norms and practices, affect health care utilization despite greater health care access. As demonstrated in Fig. 2 and 3, health care access remains a strong driver of CDI risk.

The strength of this study is the study population size. The nationwide scope allows for generalizability to the U.S. health care setting. Moreover, this study accounted for variations in antibiotic exposure risk and maximized the power to detect racial differences in CDI rates by focusing on a population at greatest risk for antibiotic exposure.

The major limitation of this study is the nature of the data. The unit of analysis is the discharge record, which does not provide information on the antibiotics prescribed or readmissions. We had to infer antibiotic exposure from bacterial infection diagnoses. Furthermore, we limited the scope of the study to antibiotic exposure in the setting of bacterial infections during hospitalizations. Another major setting for antibiotic exposure is surgical

![FIG 4](http://aac.asm.org/) (A) \textit{Clostridium difficile} infection-related mortality rates by race among patients at high risk for \textit{Clostridium difficile} infection. (B) Complicated \textit{Clostridium difficile} infection rates by race among patients at high risk for \textit{Clostridium difficile} infection. Intervals represent 95% confidence intervals.
prophylaxis, but different surgical procedures carry different risks for CDI (18), which might confound analyses of racial differences in CDI rates. We also elected to estimate antibiotic exposure risk liberally by including CDI as a diagnosis associated with increased risk for antibiotic exposure. Since we could not account for patients admitted with CDI because of outpatient antibiotic exposure or exposure to antibiotics during a different hospitalization, we included patients with CDI in the population likely exposed to antibiotics in an effort to capture the entire population at risk for antibiotic exposure. We operated on the assumption that a diagnosis of CDI represented prior antibiotic exposure, because antibiotic exposure is the most common cause of CDI. Finally, the retrospective nature of this study is a limitation, as ICD-9 diagnosis coding may be inaccurate. Given these limitations, it is difficult to exclude a genotypic effect of race on CDI rates, but we do suggest the strong possibility of health care access driving racial differences in CDI rates.

In conclusion, CDI appears to represent a deviation from the paradigm that increased health care access leads to less morbidity. Patients with higher levels of health care access are at greater risk for developing CDI, through increased cumulative exposure to antibiotics or health care settings. White race appeared less likely to be a risk factor for CDI, whereas higher socioeconomic status appeared to be associated with greater risk for CDI. The findings of this study highlight the importance of judicious and appropriate antibiotic use. Antibiotic stewardship programs are crucial for enhancing and disseminating expertise to decrease unnecessary and dangerous antibiotic exposures. This should not be limited to inpatient settings, given the existence of community-acquired CDI. Although health care access appears to be a significant risk factor for CDI, we have not completely excluded a genotypic effect of race. Future research on racial susceptibility to CDI should investigate differences in colonic microflora in relation to diet or antibiotic susceptibility patterns.

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