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Association between Socioeconomic Status and Incidence of Community-Associated *Clostridioides difficile* Infection — United States, 2014–2015

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Conflict of Interest

G.D. is a member of an advisory network for Roche Molecular Diagnostics. M.K. is a board member for the Infectious Diseases Consulting Corporation, has been a consultant for Pfizer, and received personal fees from WebMD. M.K. also reports travel support from Council of State and Territorial Epidemiologists (CSTE), Society for Healthcare Epidemiology of America (SHEA), Infectious Diseases Consulting Corporation (IDCC), WebMD, Pfizer, and Public Health Association of Australia, outside the submitted work. No other author has potential conflicts.

Abstract

We evaluated the association between socioeconomic status (SES) and community-associated *Clostridioides difficile* infection (CA-CDI) incidence across 2474 census tracts in 10 states. Highly correlated community-level SES variables were transformed into distinct factors using factor analysis. We found low SES communities were associated with higher CA-CDI incidence.

Keywords

Community-associated *Clostridioides difficile*; social determinants of health; health disparities

BACKGROUND

Traditionally a healthcare-associated infection, *Clostridioides difficile* infection (CDI) has increasingly emerged in communities, with community-associated (CA) CDI comprising 48% of all CDI cases in 2017 [1]. CA-CDI occurs in younger patients without recent hospitalizations and approximately 40% of CA-CDI cases have no recent antibiotic exposures [2, 3]. Additionally, up to 80% of cases had recent outpatient healthcare exposures; thus, while outpatient healthcare utilization may be a driver for CA-CDI, not all cases have this exposure [3]. Currently, little is known about the communities where CA-CDI is occurring and the social determinants of health that influence its spread. In this exploratory analysis, we sought to identify community-level socioeconomic status (SES) variables that are associated with CA-CDI incidence.

METHODS

CDC's Emerging Infections Program (EIP) conducts CDI surveillance in 35 counties across 10 states (Supplementary Material 1). A CDI case was defined as a positive *C. difficile* toxin or molecular assay from a person ≥1-year-old without a positive test in the prior eight weeks. Medical records were reviewed for all cases in eight EIP sites; in two EIP sites (Colorado and Georgia), medical review was performed on all cases aged 1–17 years and on a 33% random sample of cases aged ≥18 years. Cases were classified as community-associated if the *C. difficile*-positive stool specimen was collected as an outpatient or within three days of hospitalization and there was no admission to a healthcare facility in the preceding 12 weeks. All surveillance area laboratories were surveyed to determine the proportion of cases diagnosed by a nucleic acid amplification test (NAAT).

2014–2015 CA-CDI case addresses were geocoded to 2010 census tracts. Population denominators were obtained from the 2010 US census. Census tract-level SES variables were obtained from the 2011–2015 American Community Survey and the Health Research and Services Administration and chosen for inclusion based on previous studies of health disparities and known CA-CDI risk factors (Table 1) [2, 4, 5].

Case counts and population denominators were stratified based on sex, age (1–44 years, 45–64 years, and ≥65 years), and race (white only versus all other). The population denominators for the stratum aged ≥18 years in Colorado and Georgia were reduced to

33% to account for sampling. We determined the percentage of CA-CDI cases within a county that had antibiotic use (a known primary CA-CDI risk factor) in the preceding 12 weeks. Missing race (19.4% of CA-CDI cases) was imputed based on the known distribution of race by age, sex, antibiotic usage, and surveillance site. Missing antibiotic usage (5.3% of CA-CDI cases) were imputed based on the distribution of known antibiotic usage by age, sex, race, and surveillance site.

Pearson correlation coefficients were used to measure the associations between community-level (i.e., census tract-level) SES variables to identify any collinearity. Because 53% of the significant pairings of SES variables were found to be highly correlated, exploratory factor analysis was used to reduce the dimensionality and collinearity among the SES variables by identifying a small set of factors that explain the variance among the observed variables (Supplementary Material 2).

To account for census tract-level clustering effects, we used a negative binomial generalized linear mixed model to evaluate the associations of the identified factors and medically underserved area (MUA) data with CA-CDI incidence, adjusting for age, sex, race, and antibiotic and NAAT usage. Rate ratios (RR) and 95% confidence intervals (CIs) were calculated. A sensitivity analysis was performed excluding Colorado and Georgia. Analyses were performed using SAS 9.4 (SAS Institute, Cary, NC).

The surveillance protocol underwent ethical review by CDC and EIP sites and either was deemed non-research or an institutional review board approval with a waiver of informed consent was obtained.

RESULTS

During 2014–2015, 9682 CA-CDI cases were identified; of which, 9413 (97.2%) were successfully geocoded and included in the analysis.

Of 9413 CA-CDI cases, 62.4% were female, 81.4% were white, and 35.1% were aged ≥65 years (median, 56 years; range, 1–105). Most cases (59.5%) reported antibiotic use in the prior 12 weeks and median county-level percentage of cases diagnosed by NAAT was 82.1% (range, 37.7–100%).

The total surveillance area included 2474 census tracts. After adjusting for sampling methods in Colorado and Georgia, the total surveillance population was 7.9 million. The overall crude annual CA-CDI incidence was 59.4 per 100,000 persons. The crude annual incidence per census tract ranged from 5.8 to 470.7 per 100,000 persons.

Exploratory factor analysis identified a three-factor model that accounted for 95% of the observed variance (Supplementary Material 2). Three SES variables were removed due to poor factor loading. The three final factors consisted of 12 SES variables, hereafter referred to as “Poverty,” “Foreign Born,” and “High Income” (Table 1).

In multivariate analysis, the “Poverty” Factor (RR, 1.19; 95% CI, 1.15–1.22) and the “Foreign Born” Factor (RR, 1.05; CI, 1.02–1.08) were significantly associated with higher

CA-CDI incidence (Supplementary Material 3). The “High Income” Factor was significantly associated with lower CA-CDI incidence (RR, 0.95; CI, 0.92–0.97). We found similar results in our sensitivity analysis (Supplementary Material 4).

DISCUSSION

This analysis is the largest to date that examines the association between community-level SES variables and CA-CDI. Similar to previous studies [6, 7], we found that communities with lower SES had a higher CA-CDI incidence, specifically neighborhoods that have households with low income or that are receiving public assistance income, or residents living below the poverty level, who are unemployed, or who have public health insurance. Additionally, communities with people who are foreign-born or speak less English at home or with crowding in homes have a higher CA-CDI incidence.

Living in an impoverished community may be a proxy for certain outpatient healthcare exposures that could increase CA-CDI risk. Hudspeth et al. found that census tracts with higher percentages of uninsured residents had a higher CA-CDI incidence [6]. Uninsured, or underinsured, individuals may be more likely to use emergency departments to access healthcare, which has been hypothesized as a high-risk healthcare setting for facilitating *C. difficile* spread due to higher patient volumes and increased potential for exposure to symptomatic CDI patients and contaminated environments [3,8]. Notably, a case-control study found that a recent emergency department visit was an independent risk factor for CA-CDI [3].

Household crowding, a well-known risk factor for many infectious diseases, has also been found to be a risk factor for CA-CDI [8]. This is unsurprising since *C. difficile* is often acquired via the oral-fecal route, persists in the environment, and spreads more easily in crowded living conditions. Studies of CDI case households found up to 13% of household contacts, as well as the environment, most commonly the bathroom, were positive for *C. difficile* [9, 10]. Asymptomatic *C. difficile* carriers can be a source of CA-CDI, potentially increasing person-to-person transmission within a crowded household.

Foreign-born populations and those with less English speaking at home may have poor health literacy, including an inadequate understanding of the CDI risk associated with antibiotic use, secondary to language barriers. Cultural differences may also exist regarding outpatient healthcare utilization and diet that could increase the risk of *C. difficile* acquisition and disease. *C. difficile* has been isolated from several foods, although the effect of diet composition on CDI susceptibility is unknown [11]. Communities may differ in readily available food types and food affordability, which could explain some of the relationships with CDI.

This analysis was a first step to identify the types of communities in which CA-CDI is emerging. Previous studies have shown that community-level SES variables can be used to monitor health disparities in the absence of individual-level SES information [12]. It is unclear to what extent our findings represent the effect of individual differences in CDI risk

due to characteristics such as poverty, or community-level effects of resources available, or a combination of individual and community-level effects.

A major strength of our analysis is the population size and geographical diversity of the EIP sites, which have similar demographics as the U.S. population. Another strength is the use of factor analysis to evaluate many highly collinear SES variables. Collinearity is a common issue when analyzing SES information given the complex relationship between SES variables and health disparities.

Our analysis had several limitations. It is possible that some of the CA-CDI cases diagnosed by NAAT were only colonized with *C. difficile,* instead of having active disease, as NAAT detects the presence of the toxin gene, not the toxin itself. Some cases may have been misclassified as community-associated due to lack of documentation of prior hospitalizations. Since we transformed highly correlated SES variables into distinct factor scores, we could not determine the association of each underlying SES variable with CA-CDI. We were unable to control for antibiotic usage at the census-tract level and had to aggregate at the county-level, due to some census tracts having few or no cases. Additionally, we used census tract-level MUA designations as a proxy for healthcare access, though this may not have adequately controlled for outpatient healthcare utilization.

In conclusion, we found low SES communities were associated with higher CA-CDI incidence. Understanding the mechanisms by which SES factors impact CA-CDI incidence can help inform prevention strategies in these communities.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Community-Level Socioeconomic Status Variable Definitions and Exploratory Factor Analysis Results showing Final Factor Composition

Socioeconomic Status Variable (definition)	Factor 1 "Poverty"	Factor 2 "Foreign-Born"	Factor 3 "High Income"
Low Income (% households with income <$25,000 [approx. <50% of median US household income])	**0.88**	0.18	−0.18
Poverty (% persons below poverty level in past 12 months)	**0.87**	0.25	−0.17
Public Insurance (% persons with public health insurance coverage)	**0.78**	0.11	−0.28
Unemployment (% persons aged ≥16 years within the civilian work force that are unemployed)	**0.73**	0.02	−0.21
Public Assistance Income (% households who have received public assistance income in the past 12 months)	**0.71**	0.02	−0.10
Private Insurance (% persons with private health insurance coverage)	**−0.75**	−0.43	0.38
Less English-speaking at home (% persons ≥5 years who speak English at home either "not at all" or "not well")	0.16	**0.92**	−0.05
Foreign-born status (% persons who are foreign-born)	−0.01	**0.90**	0.14
Crowding (% occupied households with >1 person/room)	0.27	**0.76**	−0.10
High Income (% households with income ≥ $200,000 [approx. ≥400% of median US household income])	−0.34	−0.11	**0.80**
Expensive Homes (% of owner-occupied housing units ≥$750,000 [approx. ≥400% of median value])	−0.09	0.18	**0.70**
High Education (% people aged ≥25 years with at least bachelor's degree)	−0.51	−0.20	**0.69**
Low Education (% people aged ≥25 years with <12th grade education [includes 12th grade, no diploma])	Equal loading on more than one factor		
Health Insurance (% persons with health insurance coverage)	Equal loading on more than one factor		
New Mothers (% women aged 15–50 years who had a birth in the past 12 months)	Factor loading less than 0.5 for all factors		
Medically underserved area * (based on % of population with income below poverty level, % of population with age >65 years, infant mortality, and availability of primary care providers)	Considered a marker for healthcare exposure and excluded from factor analysis in order to evaluate its independent association with CA-CDI incidence		

* Data source: Health Resources and Services Administration. All other variables were obtained from the 2011–2015 American Community Survey.