**ABSTRACT**

**Introduction**: The prevalence of *Clostridium difficile* infection is rapidly increasing worldwide, but prevalence is difficult to estimate in developing countries where awareness, diagnostic resources, and surveillance protocols are limited. As diarrhea is the hallmark symptom, we conducted a systematic review and meta-analysis to determine the prevalence and incidence of *C. difficile* infection in patients in these regions who presented with diarrhea.

**Methods**: We conducted a systematic literature search of MEDLINE/PubMed, Scopus, and Latin-American and Caribbean Health Sciences Literature databases to identify and analyze data from recent studies providing prevalence or incidence rates of *C. difficile*-associated diarrhea in developing countries within four regions: Africa–Middle East, developing Asia, Latin America, and China. Our objectives were to determine the current prevalence and incidence density rates of first episodes of *C. difficile*-associated diarrhea in developing countries.

**Results**: Within the regions included in our analysis, prevalence of *C. difficile* infection in patients with diarrhea was 15% (95% CI 13–17%) (including community and hospitalized patients), with no significant difference across regions. The incidence of *C. difficile* infection in 17 studies including this information was 8.5 per 10,000 patient-days (95% CI 5.83–12.46). Prevalence was significantly higher in hospitalized patients versus community patients (*p* = 0.0227).

**Conclusion**: Our prevalence estimate of 15% is concerning; however, low awareness and inconsistent diagnostic and surveillance protocols suggest this is markedly underestimated. Enhanced awareness and management of *C. difficile* infection in patients with diarrhea, along with improvements in infection control and surveillance practices, should be implemented to reduce prevalence of *C. difficile*-associated diarrhea in developing countries.

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INTRODUCTION

The incidence of *Clostridium difficile* infection has greatly increased in recent years as new strains have emerged and antimicrobial resistance has increased (i.e., hypervirulent *C. difficile* ribotype 027 and ribotype 078) [1–7]. Precise global epidemiologic data are difficult to obtain, due to continually changing prevalence data and variations in surveillance practices. One recent US analysis estimated 453,000 *C. difficile* cases, 29,000 deaths, and a healthcare-related incidence of 92.8 per 100,000 persons [8]. European epidemiologic data indicate wide variation in reported incidence of *C. difficile* infection [9]. The survey of hospitalized patients in 97 institutions reported a weighted mean incidence of 4.1 per 10,000 patient-days, with individual country rates ranging from 0 to 36.3. In Latin America, Asia, and Africa, recent and comprehensive epidemiologic data on *C. difficile* infection are limited [1, 10].

Commonly associated with antibiotic use [4, 11–13], *C. difficile* was previously regarded primarily as a nosocomial infection [11, 14]; however, community-acquired *C. difficile* has now emerged as a significant public health threat [3, 8, 11, 14–16]. The epidemiology of community-acquired infection is not well understood [17]. While both nosocomial and community-acquired infection can be severe and even fatal, patients with community-acquired infection often do not have the risk factors (e.g., age ≥ 65, treatment with antibiotics, certain comorbidities) known to be associated with nosocomial infection [11, 13, 14, 17, 18].

*Clostridium difficile*-associated diarrhea (CDAD) is the hallmark symptom of clinical infection and can range in severity from mild diarrhea to fulminant colitis [12, 15]. *C. difficile* is recognized as a leading cause of healthcare-associated diarrhea [11, 19] and as the main contributing factor in gastroenteritis-associated hospitalizations and deaths [12, 20]. Mortality associated with CDAD is high, particularly in patients ≥ 65 years with comorbid conditions, severe disease, or hypervirulent strains [21].

In developing countries, surveillance data on *C. difficile* infection are not readily available, likely due to limitations in awareness, laboratory capacity and capabilities, and surveillance systems [22–24]. A recent review of the burden of *C. difficile* infection in developing countries noted that patients with diarrhea are not routinely tested for this pathogen, and, when tested, it is very often with enzyme immunoassay (EIA) rather than stool culture [25]. Clinical Practice Guidelines for *C. difficile* note that EIA is less sensitive than stool culture and is therefore an inferior alternative [11, 19]. As *C. difficile* has become resistant to many antimicrobials [1, 10], prevention of infection through the implementation of infection control and hospital epidemiology programs must be a priority [11]. With a better understanding of the epidemiologic trends related to CDAD, enhanced approaches to the prevention and control of *C. difficile* infection and associated diarrhea may be achieved. The primary objective of this systematic review and meta-analysis was to determine the current prevalence of CDAD first episodes (nosocomial or community-acquired) in developing countries. The secondary objective was determination of hospital incidence rates (cases per 10,000 patient-days) within the same case parameters.

METHODS

Search Strategy and Selection Criteria

We conducted a systematic literature search of the MEDLINE/PubMed, Scopus, and Latin-American and Caribbean Health Sciences Literature (LILACS) databases for studies providing prevalence or incidence rates of CDAD in developing countries. While there is no uniformly adopted definition of “developing countries,” it is generally accepted that this classification includes low- to middle-income countries. For the purposes of our analysis, we included such countries from four different regions: Africa–Middle East (AfME), developing Asia (Asia), Latin America (LATAM), and China. The full list of countries/territories is in Table 1.

To quantify the current burden, our search was limited to publications from January 2000 to December 2017. No language restrictions were applied; however, we required that at least the abstract of a paper be available in English in order for it to be included in our full analysis.
Details of our search strategy, including specific search terms and strings, are described in the Supplementary Materials.

To capture both nosocomial and community-acquired CDAD, the selected studies included cases in hospitalized patients and/or outpatients. We also considered factors such as whether the cases occurred during a known outbreak period, and age groups covered by the studies (adult, pediatric, or both). Clinical data were extracted from each study for analysis.

Review articles and other publications citing data from more than one study were not included; however, their citations were used to identify individual studies that had not already been identified in the literature search. Studies were included if they provided prevalence (proportion) data and/or estimated incidence density rates (cases per 10,000 patient-days). Studies were excluded if they included only recurrent or asymptomatic cases, if there was evidence of explicit selection bias (e.g., unclear denominator), or if they considered rates of admissions and/or discharges (unless they also considered patient-days).

The decision for inclusion of each study was made by Drs. Fernández and Correa, functioning as independent reviewers and screening the studies by title and abstract. Resolution of any differences was determined by Dr. Curcio.

**Assessment of Study Quality**

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) model [26] in structuring our literature analysis. In the context of our meta-analysis, the main source of quality variation results from the biases introduced during the selection of patients (e.g., when the denominator is smaller than the sum of all symptomatic cases). Because the presence of this type of selection bias has been used as an exclusion criterion in our analysis, it is assumed that the studies we selected are relatively homogeneous in quality.

**Statistical Analysis**

For the primary analysis of prevalence of CDAD, studies that provided information on the proportion of occurrence were included. The secondary objective of incidence density rate (cases per 10,000 patient-days) was analyzed on the studies providing incidence data. A subanalysis was also carried out on the prevalence data, stratifying studies across the four specified geographic regions (Table 1). An overall effect-size analysis was also performed using the incidence density rate data.

The potential for publication bias was evaluated using a funnel plot as a graphical method.
to determine the trials’ effect estimates of effect size against the measure of precision for all included studies [27]. We also utilized the Egger linear regression test for funnel plot asymmetry, which may be indicative of bias in meta-analyses [28].

A meta-regression analysis, which is generally performed to identify relationships between dependent and independent variables across studies and/or subgroups [29], was conducted relevant to the route of *C. difficile* acquisition, geographic regions, occurrence during known outbreaks, and age groups. For those covariates demonstrating statistical significance in the meta-regression analysis, a subanalysis was conducted.

Because a proportion as an effect to be measured raises particular concerns, a funnel plot was used for the meta-analysis to stabilize variances across studies prior to pooling the data [30, 31]. In contrast, the logarithmic transformation of the variable was used to analyze the incidence density values [32]. The random effects model was utilized for the global effect size when significant heterogeneity across studies was shown.

For the statistical analysis of the values expressed as a proportion, the Metaprop package in R software (v.3.4.2) was used. For the analysis of the values expressed as incidence, the implementation of the transformation suggested by Stijnen et al. [32] was used from the Metafor package of the same R software.

**Compliance with Ethics Compliance**

This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

**RESULTS**

**Literature Selection**

As shown in Fig. 1, the initial literature search in MEDLINE/PubMed, Scopus, and LILACS yielded 421 results, 51 of which were identified from a meta-analysis conducted by Borren and colleagues [33]. After removal of duplicate titles and abstracts, 204 full-text publications were screened for inclusion in the analysis, with the greatest number of articles pertaining to Asia (n = 75). Reviews of full-text articles resulted in another 115 exclusions, giving a total of 89 articles were selected for inclusion in our systematic review and meta-analysis.

**Publication Bias Analysis**

The funnel plot and the Egger test for funnel plot asymmetry (p < 0.001) both demonstrated significant publication bias, indicating a high variability across the studies included in our analysis (Fig. 2).

**Meta-Analysis**

Based on the 85 studies in this meta-analysis that included prevalence data (Fig. 3) [34–118], among patients in developing countries with
diarrhea, a first episode of *C. difficile* infection was determined to be the cause in 15% of cases (95% CI 13–17%) (including community and hospitalized patients). In the 17 studies that included incidence data (Fig. 4), the incidence density rate of *C. difficile* infection among patients with diarrhea was 8.5 per 10,000 patient-days (95% CI 5.83–12.46).

A stratified subanalysis of the prevalence studies by geographic regions (Fig. 5) showed that, among patients with diarrhea, a first episode of *C. difficile* infection was present in 19% in LATAM (95% CI 13–27%), 11% in AFME (95% CI 7–18%), 12% in Asia (95% CI 10–15%), and 20% in China (95% CI 16–25%). There were no statistically significant differences across regions.

**Meta-Regression Analysis**

The only covariate demonstrating statistical significance in the meta-regression analysis was the route of CDAD acquisition (Table 2). In studies including only hospitalized patients, the values of the ratio were significantly higher than in studies including community-acquired cases or both nosocomial and community-acquired [\(p = 0.0227\) (95% CI 0.0165–0.2196)]. Based on this finding, a subanalysis of prevalence by route of acquisition was conducted on studies including acquisition data. As shown in Fig. 6, among patients presenting with diarrhea, *C. difficile* infection was significantly more prevalent in studies involving hospitalized patients [17% (95% CI 15–19%)] versus studies including community patients [4% (95% CI 1–9%)] or both [8% (95% CI 6–11%)]. While we intended to examine CDAD prevalence and incidence by age, we found very few studies that clearly stratified by age groups. Our subgroup meta-analysis showed a prevalence of 12% for pediatric patients, and 16% prevalence for adults; however, the scarcity of pediatric data made it impossible to determine an age-related trend.

**DISCUSSION**

In this meta-analysis of CDAD in developing countries, we found 15% of diarrhea cases to be attributable to *C. difficile* infection (including community and hospitalized patients). The proportions were highest in LATAM and China, but there was no significant difference across regions. This study outcome was specific to determining the cause of diarrhea in patients presenting with this symptom. Due to inconsistencies in study designs, comparisons to other parts of the world are not always easily drawn, and lower prevalences of *C. difficile* infection in patients with diarrhea have been observed (range 7.4–12.7%). For example, in a prospective analysis of 4659 fecal samples from inpatients in the United Kingdom with suspected antibiotic-associated diarrhea, *C. difficile* was determined to be the causative pathogen in
Fig. 3 Meta-analysis of prevalence of CDAD based on the 85 studies including prevalence data

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12.7% of cultures [119]. A Berlin study that included analysis of 693 cultures from inpatients with antibiotic-associated diarrhea detected *C. difficile* in 11.4% of samples [120]. A smaller study conducted at a major hospital in Houston, Texas, USA, found *C. difficile* to be the causative pathogen in 7.4% of 81 inpatients experiencing diarrhea [121]. Based on these limited data, the prevalence of CDAD is higher in the developing countries included in our study.

Similarly, the incidence of *C. difficile* infection among patients with diarrhea in developing countries, which we determined to be 8.5 per 10,000 patient-days (95% CI 5.56–11.79), is not easily compared to incidence rates in more developed regions such as the US and Europe. However, this undoubtedly low incidence rate is approximately twice that reported in Europe. The hospital-based European survey noted above resulted in a weighted incidence of 4.1 per 10,000 patient-days, with considerable variation in individual country rates [9]. It was noted that factors such as diagnostic procedures and capabilities were inconsistent, making it difficult to compare epidemiologic trends across countries within this survey. US data from the 2011 survey referenced above indicate a mean crude incidence of 9.3 and 4.8 per 10,000 persons for healthcare-associated and community-acquired *C. difficile* infection, respectively [8]. A report from the US Centers for Disease Control and Prevention estimated the mean crude incidence for *C. difficile* infection in 2015 to be 14.9 per 10,000 persons (8.3 and 6.6 for healthcare-associated and community-acquired infection, respectively) [122]. While the US rate of 14.9 per 10,000 persons appears to be comparable to that of developing countries in our analysis, we must recognize that we would expect reported rates to be higher in developed regions where *C. difficile* infection is more proactively assessed and managed.

**Fig. 4** Meta-analysis of incidence of CDAD based on the 17 studies including incidence data.
Fig. 5 Prevalence of CDAD stratified by region
Although we found no statistically significant differences in prevalence across regions, due to numerous factors related to diagnosis and management, it may be reasonably assumed that prevalence might be underestimated. It has been observed that awareness of *C. difficile* as a cause of diarrhea is relatively low in developing regions such as Asia and Latin America [22, 123]. For example, a 2015 survey of physicians in Latin American countries reported low-to-moderate knowledge of *C. difficile* diagnosis and management [124]. Similarly, a survey of physicians in Taiwan found marked differences between internationally accepted treatment guidelines for *C. difficile* and actual clinical practice [125]. In addition, diagnostic capacity and capabilities in developing countries are generally suboptimal [22, 23, 124, 126]. Thus, CDAD is likely under-recognized and insufficiently managed in these regions.

Our meta-regression analysis found the route of acquisition to be the only prespecified variable to demonstrate a statistically significant difference, with the value of the ratio for CDAD being higher in hospitalized patients than in community patients. Our subanalysis corroborated this finding, showing the prevalence of CDAD to be significantly higher in studies including only hospitalized patients versus those including community patients or both. A number of factors may be contributing to this finding. The risk of hospital-acquired infections such as *C. difficile* is greater in developing countries, which lack resources for effective infection control programs [127, 128]. Hospitalized patients are more likely to have the recognized risk factors for *C. difficile* infection, namely advanced age, antibiotic use, and certain comorbidities. Prescribing rates for antibiotics, particularly those strongly associated with *C. difficile* infection (e.g., cephalosporins, fluoroquinolones), are higher in the developing countries than in other regions [129].

While the data on healthcare-acquired CDAD are salient, it is important to consider that community acquisition is a relatively new trend that until recently has not been a focus of epidemiologic research. Of the 85 studies included in our analysis that provided prevalence data, only 12 included cases of community-acquired CDAD (7 included both hospital-acquired and community-acquired cases). This under-surveillance is likely masking a higher rate of community-acquired disease in these developing countries. In areas where surveillance is more aggressive, proportions of community-acquired CDAD have been shown to be much higher. In the US, for example, community onset accounted for almost 50% of *C. difficile* infections in 2010 [2].

### Table 2: Summary of meta-regression analysis

| Variable                          | Value   | Coefficient | 95% CI       | p value |
|-----------------------------------|---------|-------------|--------------|---------|
| Route of acquisition (ref = Both) | Community | −0.0600     | −0.2088 to 0.0888 | 0.4290 |
|                                   | Hospital | 0.1181      | 0.0165 to 0.2196 | 0.0227 |
| Outbreak (ref = No)               | Yes     | −0.0265     | −0.2860 to 0.2329 | 0.8413 |
| Age group (ref = Adult)           | Both    | −0.0463     | −0.1280 to 0.0355 | 0.2676 |
|                                   | Pediatric | −0.0832    | −0.2267 to 0.0603 | 0.2556 |
|                                   | Unknown | −0.2065     | −0.4719 to 0.0589 | 0.1272 |
| Region (ref = AfME)               | Asia    | −0.0345     | −0.1184 to 0.0494 | 0.4205 |
|                                   | China   | 0.0518      | −0.0508 to 0.1543 | 0.3226 |
|                                   | LATAM   | 0.0611      | −0.0367 to 0.1589 | 0.2209 |

Coefficients, confidence intervals for coefficients and p values for variables in meta regression. Studies including exclusively hospital-acquired CDAD showed a significant positive value. The remaining variables had non-significant coefficients.
| Study | Events | Total |
|-------|--------|-------|
| Hosp. Com = Hospital | 5 | 90 |
| Forsin 2003 [46] | 5 | 90 |
| Garea 2007 [71] | 55 | 105 |
| Zambello-Sales 2008 [58] | 31 | 104 |
| Rebecsnow 2010 [10] | 43 | 218 |
| Seco 2014 [49] | 4 | 74 |
| Spadler 2014 [41] | 64 | 439 |
| Place-Durais 2016 [42] | 81 | 962 |
| Martin-Olmos 2016 [48] | 78 | 285 |
| Garcia 1988 [44] | 11 | 80 |
| PIturba 2015 [45] | 22 | 150 |
| Arzarel 2001 [46] | 26 | 92 |
| Stepanski 2010 [41] | 46 | 369 |
| Al-Tawfiq 2011 [46] | 42 | 913 |
| Hasheem 2012 [93] | 99 | 443 |
| Abu-Faddal 2014 [93] | 17 | 72 |
| K-mediated 2015 [93] | 35 | 150 |
| Jonasson 2014 [68] | 8 | 176 |
| Vlahovnath 2013 [51] | 4 | 25 |
| Hus 2006 [98] | 6 | 48 |
| Kivisch 2007 [96] | 150 | 559 |
| Chaudhary 2008 [90] | 37 | 525 |
| Var-2006 [91] | 386 | 3609 |
| Jostly 2009 [62] | 36 | 214 |
| Chi 2010 [46] | 37 | 146 |
| Chen 2011 [64] | 268 | 2212 |
| Chang 2013 [65] | 380 | 2440 |
| Inglis 2011 [95] | 17 | 99 |
| Lee 2012 [97] | 8 | 80 |
| Haidar Naja 2012 [98] | 57 | 191 |
| Hesse 2012 [91] | 24 | 175 |
| Inglis 2013 [70] | 12 | 150 |
| Kasirwan 2013 [71] | 5 | 50 |
| Vakkili 2010 [75] | 532 | 3044 |
| Ravindranath 2015 [76] | 7 | 172 |
| Vakkili 2015 [79] | 174 | 1170 |
| Huw 2013 [78] | 41 | 277 |
| Hame 2013 [76] | 21 | 70 |
| Zhou 2014 [60] | 63 | 204 |
| Hoang 2014 [81] | 90 | 240 |
| Fang 2014 [82] | 7 | 20 |
| Wang 2014 [83] | 31 | 124 |
| Delhyski 2015 [84] | 31 | 111 |
| Chen 2016 [85] | 94 | 339 |
| Qin 2016 [96] | 178 | 768 |
| Ju 2017 [87] | 397 | 3853 |
| Perera-Dam 2017 [88] | 178 | 768 |
| Routligc-Vanis 2017 [89] | 6 | 43 |
| Convair 2017 [90] | 36 | 203 |
| Satozur 2017 [91] | 75 | 775 |
| Criela 2017 [92] | 48 | 48 |
| Ofate-Gutierrez 2016 [93] | 29 | 325 |
| Kulla 2017 [94] | 418 | 1908 |
| Arnedo 2016 [95] | 19 | 165 |
| Sen Pi 2017 [96] | 21 | 210 |
| Rezaelez-Zahed 2017 [97] | 46 | 233 |
| Politek 2016 [98] | 100 | 422 |
| Colfie 2017 [99] | 37 | 340 |
| Li 2017 [100] | 32 | 365 |
| Ju 2017 [102] | 46 | 521 |
| Yon 2017 [103] | 61 | 641 |
| Shi 2008 [104] | 285 | 1059 |
| Chen 2009 [105] | 37 | 489 |
| Kim 2010 [106] | 196 | 769 |
| Yang 2014 [107] | 330 | 1435 |
| Li 2016 [108] | 93 | 500 |
| Sheshadri 2021 [109] | 29 | 300 |
| Ieier 2020 [110] | 9 | 77 |
| Alemper 2019 [111] | 8 | 77 |
| Hsu 2011 [112] | 304 | 3739 |
| Teppeh-Naeh 2011 [113] | 31 | 255 |
| Thanikoon 2016 [116] | 581 | 3851 |
| Chou 2017 [117] | 2 | 100 |
| Sadeghi-Fardi 2012 [118] | 57 | 942 |

| Proportion | 95% CI | Weight (fixed) | Weight (random) |
|------------|--------|----------------|-----------------|
| 0.06 | [0.02, 0.12] | 0.2% | 1.1% |
| 0.35 | [0.28, 0.43] | 0.3% | 1.2% |
| 0.30 | [0.21, 0.49] | 0.2% | 1.1% |
| 0.20 | [0.15, 0.30] | 0.5% | 1.2% |
| 0.14 | [0.07, 0.23] | 0.1% | 1.1% |
| 0.15 | [0.11, 0.19] | 0.8% | 1.2% |
| 0.21 | [0.17, 0.27] | 0.7% | 1.2% |
| 0.37 | [0.22, 0.32] | 0.6% | 1.2% |
| 0.11 | [0.07, 0.15] | 0.1% | 1.1% |
| 0.14 | [0.07, 0.21] | 0.2% | 1.1% |
| 0.28 | [0.19, 0.39] | 0.2% | 1.1% |
| 0.27 | [0.20, 0.34] | 0.5% | 1.2% |
| 0.12 | [0.11, 0.14] | 3.8% | 1.3% |
| 0.13 | [0.11, 0.14] | 1.1% | 1.3% |
| 0.24 | [0.14, 0.35] | 0.1% | 1.1% |
| 0.12 | [0.10, 0.15] | 0.1% | 1.1% |
| 0.10 | [0.04, 0.18] | 0.1% | 1.1% |
| 0.04 | [0.02, 0.03] | 0.3% | 1.2% |
| 0.07 | [0.05, 0.09] | 0.3% | 1.2% |
| 0.12 | [0.08, 0.17] | 0.4% | 1.2% |
| 0.12 | [0.09, 0.19] | 0.2% | 1.1% |
| 0.10 | [0.09, 0.19] | 0.3% | 1.2% |
| 0.15 | [0.11, 0.20] | 0.1% | 1.1% |
| 0.07 | [0.05, 0.10] | 0.9% | 1.3% |
| 0.07 | [0.05, 0.09] | 0.9% | 1.3% |
| 0.11 | [0.10, 0.20] | 0.1% | 1.1% |
| 0.12 | [0.08, 0.17] | 0.4% | 1.2% |
| 0.07 | [0.05, 0.10] | 0.5% | 1.2% |
| 0.09 | [0.06, 0.10] | 0.3% | 1.2% |
| 0.10 | [0.05, 0.13] | 1.1% | 1.3% |
| 0.10 | [0.05, 0.13] | 0.4% | 1.2% |
| 0.10 | [0.05, 0.13] | 1.3% | 1.3% |
| 0.10 | [0.05, 0.13] | 1.1% | 1.3% |
| 0.10 | [0.05, 0.13] | 1.3% | 1.3% |

**Fig. 6** Subanalysis of significant covariate: prevalence by mode of CDAD acquisition
Study limitations include, as previously noted, the potential for significant publication bias related to high variability among the studies selected. Publication bias in meta-analyses is often attributable to the number of included studies being lower than the total number of studies conducted [27]. By closely adhering to the PRISMA model in selecting studies for inclusion [26], we feel we have minimized this concern. However, the definition of CDAD according to microbial testing may have varied across studies. Inconsistencies in study designs also make it challenging to compare prevalence in developing countries to that in more developed areas, such as the US and Europe. Along those lines, wide variation in diagnostic protocols and surveillance practices would suggest that prevalence and incidence of CDAD are underestimated. In addition, in most of the included studies in our meta-analysis, populations were poorly defined, which might make comparisons unclear.

We found no data related to CDAD in long-term care facilities, which would now be included under the umbrella of nosocomial acquisition. We found only 17 articles with data on incidence rates, which makes that aspect of the analysis underpowered.

CONCLUSION

Low awareness of CDAD in developing countries and inconsistent surveillance protocols likely cause marked underestimates of prevalence and incidence rates in developing countries. In this meta-analysis, we estimated prevalence of *C. difficile* infection to be 15% in patients with diarrhea; however, this should be considered the tip of the iceberg in light of limited diagnostic resources and protocols, as well as the low level of awareness, in developing countries. Hospital-acquired CDAD was found to be a greater concern than community-acquired disease, although the latter is undoubtedly trending upward. Heightened awareness of CDAD among healthcare providers; as well as enhancements in diagnostic capabilities, infection control, and surveillance protocols; should be implemented to better manage and prevent *C. difficile* infection and associated diarrhea in developing countries.

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**Compliance with Ethics Compliance.** This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

**Data Availability.** The datasets during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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