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Examining the epidemiology and microbiology of *Clostridium difficile* carriage in elderly patients and residents of a healthcare facility in southern Ontario, Canada

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SUMMARY

Background: Whereas *Clostridium difficile* has been extensively studied in acute care facilities (ACFs), there is limited information about long-term care facilities (LTCFs), despite the high occurrence of putative risk factors (e.g. age, antimicrobial use, health-care system contact).

Aim: To evaluate *C. difficile* colonization in elderly patients and residents from one ACF and its associated LTCF.

Methods: Stool swabs were collected from 884 LTCF and elderly (>65 years) hospital patients. Selective culture, polymerase chain reaction ribotyping and toxin gene characterization were performed.

Findings: *C. difficile* was isolated from 92/410 (22.4%) ACF and 89/474 (18.8%) LTCF samples. Ribotypes 027 (35%) and 020 (10.4%) predominated in the LTCF whereas ribotypes AI-82/1 (20.7%) and ribotype O (14.1%) predominated at the ACF ($P = 0.031$). In the LTCF, *C. difficile* colonization was associated with a history of proton pump inhibitor (PPI) use, and the interaction terms of male residents with prior medical leave of absence, and a prior history of *C. difficile* infection (CDI) combined with fluoroquinolone use. In the ACF, *C. difficile* colonization was associated with length of stay, feeding through a tube, antibiotic use, immunosuppressive therapy and VRE colonization, as well as the interaction terms for cephalosporin and fluoroquinolone use, prior CDI and cephalosporin use, and prior CDI and fluoroquinolone use.

Conclusion: *C. difficile* colonization by ACF and LTCF residents was common, despite a low apparent incidence of CDI. The association with PPI provides further evidence of the potential importance of this widely used drug class in *C. difficile* colonization. Wide genetic diversity was present, highlighting the likelihood of multiple unidentified routes of *C. difficile* acquisition.

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Introduction

Clostridium difficile is an important pathogen in healthcare facilities (HCFs). It is the most frequent cause of healthcare-associated infectious diarrhoea in adults and is responsible for nearly all cases of pseudomembranous colitis [1–6]. *C. difficile* is an anaerobic Gram-positive, rod shaped, spore-forming bacterium that is found in a highly oxygen-sensitive vegetative form, or in a stable spore form, that can be widely disseminated in the healthcare environment [4,7,8]. Colonized or infected patients and spore-contaminated environments have been identified as the primary reservoirs for *C. difficile* [1,4]. It is also estimated that *C. difficile* is present in the stools of 5% of healthy adults and in 30–70% of infants [8]. In a hospital setting, it is estimated to be present in as much as 20% of the population [9].

In acute care facilities (ACFs), risk factors for CDI have been extensively studied. Advanced age, underlying medical illness, antimicrobial use (particularly the use of clindamycin, cephalosporins and fluoroquinolones), immunosuppressive therapy, and prolonged length of stay have all been associated with increased risk of CDI [1,3–6]. There is comparatively limited information pertaining to CDI in long-term care facilities (LTCFs). Because of their age, frequent antimicrobial exposure, frequent contact with the acute care system and the high rate of comorbidities, residents of LTCFs should be at particularly high risk for CDI, yet objective data are rather sparse [1,3–6]. However, *C. difficile* colonization of non-diarrhoeic elderly ACF patients and LTCF residents is widespread [8,10]. Despite the high-risk nature of the LTCF population, few outbreaks of CDI have been reported. Incidence of CDI, prevalence of *C. difficile* colonization, and risk factors for infection and colonization have not been adequately investigated in this population. The relationship between hospital-associated CDI, LTCF-associated CDI and community-associated CDI is also poorly understood and it is unknown whether CDI in LTCF residents is acquired in the LTCF, or whether it occurs mostly in residents who have been recently transferred from a hospital setting [1]. Understanding the epidemiology of *C. difficile* in LTCF is critical for the development of proper disease surveillance, for understanding the burden of disease, for management of infected and colonized residents, for development of measures to reduce CDI in LTCF residents, and for reduction of the risk to acute care facilities from admission of infected or colonized LTCF residents.

Whereas there is a logical focus on CDI – the clinical manifestation of exposure to this pathogen – asymptomatic carriage is a critically important but poorly investigated area. Colonized individuals ('carriers') may be at increased risk of subsequent development of CDI and may pose a risk to others, yet this has not been adequately studied in LTCFs. The relevance of colonization is so poorly understood that arguments can be made both for beneficial and detrimental aspects of colonization. It has been suggested that colonization may protect against the development of symptomatic disease [4]; however, objective study of this topic has been limited and the positive or negative aspects of colonization on development of CDI are unclear. Further differentiating the impact of colonization on risk of CDI, versus factors that influence both colonization and CDI, is challenging. Regardless, a better understanding of colonization in populations such as LTCF residents is important to better elucidate the epidemiology and pathophysiology of CDI.

Because of the regional variation in CDI, differences in acute care and LTC systems, and the changes in the epidemiology of CDI over the past decade, contemporary and geographically relevant data are required to understand the challenges faced by LTCFs and their associated health care providers in Ontario. Identification of risk factors for colonization, the impact of colonization on the development of CDI in both colonization and CDI, could lead to early interventions and preventive measures that might improve patient outcomes and decrease cost associated with treatment.

The objectives of this study were to determine the prevalence of *C. difficile* carriage in elderly patients and residents in one ACF and its associated LTCF, and to identify risk factors for *C. difficile* colonization.

Methods

Setting

One healthcare facility, located in southern Ontario, Canada, participated in this study. The entire facility is geared towards geriatric care and consists of three distinct care facilities: a retirement residence, also widely known as an assisted living community, that accommodates 190 residents; a 472-bed nursing home (LTCF), with six floors that are designated based on the type of care that is required; and a 262-bed geriatric hospital (ACF) mostly for complex continuing care. Patient samples were collected from both the ACF and the LTCF from August 1st, 2014 to March 1st, 2015. This study was approved by the research ethics boards of the University of Guelph and the participating healthcare facility (REB#14MR022).

Sampling

Samples were collected in a cross-sectional manner from all LTCF residents and elderly ACF patients (aged ≥ 65 years), including all new admissions, over the course of the study. Dry, sterile swabs (Copan Eswabs™, Copan Diagnostics Inc., USA) were used for specimen collection. Stool swabs were collected during regular toileting or pericare by the facility's nurses. The swabs were immersed in 1 mL of Liquid Amies and FLOQSwab™ and stored at 4°C, for up to several weeks, until processing.

For each patient sampled, risk factor data were collected by the facility's staff through retrospective chart review. The data collected are listed in Table 1. Only one sample per patient was collected, with the exception of four patients from the ACF who were transferred from the LTCF during the study period. Their samples were collected at the initial sampling time in the LTCF, and upon admission to the ACF. These were tested and processed twice. Duplicate information was maintained in the data for these patients.

Processing

Selective culture for *C. difficile* was performed. Stool swabs were immersed in 10 mL of Tryptone Soy Agar (TSA) broth and incubated anaerobically at 37°C for five to seven days. A 2 mL aliquot of broth was alcohol-shocked by addition of an equal volume of anhydrous alcohol. Following a 1 h incubation period at room temperature, the samples were centrifuged at 4000 rpm for 10 min. The resulting pellet was plated onto *C. difficile*

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