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Clostridium difficile infection in elderly nursing home residents

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ABSTRACT

Age-related changes in intestinal flora and host defences, the receipt of antibiotic treatment, and the presence of underlying diseases are some of the most common risk factors associated with *Clostridium difficile* infection. Therefore, retirement care facilities for elderly people have been pinpointed as frequent sources of contamination. There is only limited data regarding the presence and epidemiology of *C. difficile* in nursing homes, and this gap in the current literature emphasises the need to gain a better understanding of the situation in order to prevent the emergence of new outbreaks among this population group.

1. Introduction

Clostridium difficile is a well-known anaerobic Gram-positive spore forming bacterium responsible for significant antibiotic-associated diarrhoea and pseudomembranous enterocolitis. Although reporting is not mandatory, the incidence of *C. difficile* infection (CDI) in hospitals has been established at both regional and national levels, ranging from 0 to 19.1 per 10, 000 patient days with an annual European economic burden estimated around €3000 million [1]. *C. difficile* related diarrhoea is frequently diagnosed among elderly residents in nursing homes and other long-term care facilities for older people [2–4]. Along with antibiotic treatment [4,5], advanced age has classically been considered to be a risk factor for *C. difficile* colonisation, and related to an increase in mortality rate [6–8].

Recent studies describe colonisation by toxigenic *C. difficile* strains as ten-times higher in nursing home residents than in the general population living outside long-term care facilities [9,10]. The deteriorating health status of nursing home residents and the typically close contact between them (including cohabitation in the same contaminated environment) promote bacterial colonisation, the development of infection and the spread of bacterial spores. In addition, the risk of *C. difficile* acquisition by nursing home residents during a hospital stay is significant [11]. Residents can also be asymptomatic carriers while still representing a potential source of contamination among other patients [9].

Here, we review the current literature data on the occurrence of *C. difficile* colonisation in nursing homes. The main factors associated with infection are also analysed, as well as the mortality rate and the genetic diversity of the isolates between different geographic areas.

2. Methods

Publications analysed were searched on PudMed (http://www.ncbi.nlm.nih.gov/pubmed) with the terms "*C. difficile* nursing homes" and "*C. difficile* elderly". Additionally, further articles were included by reviewing the references of the articles identified.

3. Occurrence of *C. difficile* in nursing homes across different countries

A relatively low number of studies have estimated the prevalence of *C. difficile* in nursing homes and other long-term care facilities for the elderly. High isolation frequencies have been described in most of the studies conducted in USA, with up to 46% of residents testing positive for *C. difficile*. In contrast, in Canada, Europe, UK, Ireland or Australia the reported rates are much lower, varying between 0.8% and 10% (Table 1). However, it is necessary to note that sample size, age, or methodologies are not standardised among the available studies, making meaningful comparison of the results difficult. Seasonal differences should be also considered: a

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Table 1
Summary data for the presence of *C. difficile* in nursing homes and other long-term care facilities for elderly people across different geographic areas.

Country	Residence of the patients enrolled in the study	*C. difficile* colonization (%)	CDI case	Asymptomatic carriers of toxigenic *C. difficile* (T) or (NT) non-toxigenic carriers (%)	Main PCR-ribotypes identified	Mean aged of colonised residents	Study period	Reference
Germany	Nursing home[a]	11/240 (4.6) (0–10)[b]	1	T 9 (81.8) NT 1 (9.1)	014 001	83	2010–2011	[9]
France	Nursing home[a]	2.39/10,000 resident-days[d]	25[c]	–	027	79.8	2006–2009	[12]
UK								
Scotland	Care home residence[a]	19/2385 (0.80)[d]	19	–	–	≥65	2008–2009	[2]
Ireland								
Cork	Continuing care institution for the elderly	10/100 (10)	0	T 7 (7) NT (3)	–	82	–	[13]
Australia								
Melbourne	Residential aged care facility[a]	1/119 (0.84)	0	T/NT 1 (0.84)	–	79.2	2010	[14]
USA								
Maryland	Long-term care facility for the elderly	119/258 (46.1)[e]	119	–	–	78.3	2005–2010	[15]
New York	Nursing home[a]	0.52–0.67/10,000 [f]resident-days	102	–	–	83	2009–2011	[11]
Virginia	Nursing home[a]	235/489 (48.1)[g]	225	NT 10 (2.04)	027	–	2009	[10]
Pennsylvania	Long-term care veterans affairs	0.04–0.028/1000 resident-days	66	–	–	77	2004–2009	[16]
Ohio	Nursing home[a]	1.7–2.9/10,000 resident-days[d]	11,200	–	–	–	2006	[3]
Ohio	Long-term care facility[a]	40/73 (54.8)	5	A 35 (47.9)	027	70	2006	[17]
Rhode Island	Nursing home[a]	11/172 (6.4)[h]	11	–	–	81.4–85.8	2008	[18]
Canada								
Ontario	Nursing home	(2.1–8.1)	–	–	–	–	–	[4]

[a] More than one setting enrolled in study.
[b] Variation in *C. difficile* colonisation rate among 25 nursing homes.
[c] Only confirmed CDI 027 cases were taken into account.
[d] Results obtained from a national or regional level survey.
[e] Data from a survey conducted in a hospital reflecting the total of patients with CDI acquired in a long-term care facility in relation to the total number of hospitalised patients developing CDI.
[f] Incidence of CDI developed more than 30 days after admission.
[g] Data from nursing home residents obtained in a laboratory for *C. difficile* testing.
[h] Only patients in nursing homes with results of a urinalysis were studied.

higher number of *C. difficile* patients were observed during the winter months in a previous study conducted in Germany [19].

A reduced variability in the isolates from residential care facilities for elderly people was reported between different countries, with PCR ribotype 027 remaining the dominant type in nursing homes regardless of their location [10,17,20]. In an investigation of a large outbreak of *C. difficile* PCR-ribotype 027 infections in France from 2008 to 2009, elderly patients over 80 years old were found to be the main population affected. Some of these patients were probably transferred from hospitals to nursing homes (and vice versa) contributing to the spread of the strain [12]. In contrast, in a study conducted across 25 nursing homes in Germany, none of the isolates obtained were identified as PCR-ribotype 027, although this type had been largely isolated from hospitalised patients in this region. The authors hypothesised that this PCR-ribotype may be more related to CDI rather than asymptomatic carriage as in only one case did a resident develop the infection during the course of the study [9]. Other PCR-ribotypes most frequently found in nursing homes are 014 (accounting for between 8% and 30% of the isolates) and 001 (accounting for between 7% and 20% of the isolates) [9,10].

4. Factors associated with *C. difficile* colonisation in elderly people

Previous studies have highlighted certain factors that make people over 65 years old more susceptible to being colonised by *C. difficile* [4,5]. Antibiotic treatment and age-related changes in intestinal flora and host defences, as well as the presence of other underlying illness may promote *C. difficile* colonisation, the developing of the infection and (in some cases) further recurrences [21,22]. One previous study evaluating factors associated with *C. difficile* acquisition in residents of a nursing home found no apparent relationship between infection and dementia, incontinence, contact with other residents with diarrhoea or age over 82 years. However, the authors observed that previous CDI, hospital admission or antibiotic therapy seemed to be related to toxigenic *C. difficile* presence [9]. A further report identified no association between *C. difficile* carriage and gender, age over 65 years, the length of the hospital stay, previous infection with the bacterium or the use of proton pump inhibitors [13]. In another study of the epidemiology of CDI among elderly care home residents, the presence of a nasogastric or gastronomy feeding tube, incontinence, underlying diseases or an antibiotic treatment were identified as significant independent variables associated with the infection [35]. Antibiotic treatment has been shown to alter gut microbiota and to decrease the colonisation resistance for pathogens such as *C. difficile*, increasing the risk of developing the infection. Nevertheless, a study conducted in hospitalised patients aged 65 years or more reported 50% of the positive culture samples to be found in asymptomatic subjects with a history of an antibiotic usage (except clindamycin). Moreover, most of the strains obtained were toxigenic [23]. In the same study, a reduction in faecal microbial diversity was observed in patients with CDI but not in asymptomatic subjects from whom *C. difficile* had been isolated. Another study reported similar results with reduced numbers of *Bacteroides*, *Prevotella*, *Bifidobacteria* and an increase of facultative species such as *Clostridium* or *Lactobacillus* sp in the presence of

CDI. Although this study found a decrease in the diversity of bifidobacterial species in favour of an increase in Bacteroides species in the faeces of healthy elderly people, the authors also found the microbiota of elderly patients with CDI markedly different from those without colonisation [24].

In a literature review of *C. difficile* associated small bowel enteritis involving analysis of 56 cases published from 1980 to 2010, the authors came to support the contention that immunosenescence and severe underlying disease could play a critical role in this infection [16].

On the other hand, a recent report defines prognostic markers for a complicated course of CDI, studying hospitalised patients with diarrhoea and with a positive result for the *C. difficile* toxin test. The mean age of these patients was 65 years. The study concludes that age (≥85 years), admission due to diarrhoea, diagnosis at the ICU department, recent abdominal surgery and hypotension were independent predictors of a complicated course of *C. difficile* infection [21].

5. *C. difficile* spores in room environments and contamination of nursing home residents in hospital

Several studies have reported the capacity of *C. difficile* to persist on the skin and in the room environment for between one and four weeks after therapy, and on inanimate surfaces for as long as five months [25,26]. There are few studies that refer to the presence of *C. difficile* in the environment of elderly patient hospital wards [4,27,28]. Contaminated areas of the environment such as floors, electronic thermometers and even the air can contribute towards *C. difficile* transmission in healthcare settings [4,29]. In patient rooms, the most commonly contaminated areas have been identified as bedside tables, bedrails and toilet floors [17,26,27].

Nursing home residents are often transferred to hospitals when they suffer an acute clinical problem or when they require special medical care. These situations can result in transmission of *C. difficile* strains between hospitals and nursing homes. A previous study found that approximately two-thirds of CDI cases occurred within 30 days of nursing home admission after hospitalisation [11]. An additional study states that the mean duration of hospital stay in elderly patients without *C. difficile* diarrhoea is 20 days while 75% of *C. difficile* infection cases in aged people occur by day 21 of a hospital stay. The authors conclude that CDI is, for many patients, the cause of their prolonged stay in hospital [30].

6. Mortality associated with *C. difficile* among elderly and nursing home residents

Although mortality associated with CDI is estimated at around 17%, it seems that this percentage could be higher among older people [31]. In a pooled analysis of *C. difficile* enteritis [16], authors found that age was significantly higher in the 18 (32%) non-survivors from a group of patients with a mean age of 66 years (subjects between 60 and 76 years old). The median time between the onset of *C. difficile* infection symptoms and death was 4 days. Similar finds were reported in an epidemiology survey conducted in Ohio where, within the total number of patients' deaths from CDI, mortality was consistently higher in the oldest age population [3]. Another recent study conducted in four different nursing homes in New York reported three deaths among 23 residents who develop *C. difficile* infection after more than 30 days following admission [11].

Further studies have attributed the presence of *C. difficile* PCR ribotype 027 in patients between 60 and 90 years of age with an increased likelihood of CDI related death [16,32,33]; however, studies concerning the incidence of this strain in nursing homes are limited. Besides the hypervirulent PCR-ribotype 027, other *C. difficile* types have been linked with the death of elderly patients living in long-term care facilities, such as PCR-ribotype 078. In a *C. difficile* outbreak which occurred in Irish hospitals and nursing homes, eight out of 15 subjects with PCR-ribotype 078 colonisation died, and in five of the cases the bacterium directly contributed to the death of the patients [34].

Despite these findings, other reports about CDI and related mortality in older people have not definitively established *C. difficile* as the causative agent of death [4,35]. Furthermore, in a cohort study of community-associated CDI infection among older people and the relationship between infection, antibiotic exposure, and care home residence, authors reported an increased mortality among subjects that whose infections were healthcare-onset, but not among CDI cases in the community [2]. Similarly, in the study of Garg et al. [15], the highest mortality was found among *C. difficile* infection cases in hospital (9.4%) while the percentage of deaths was lower in long-term care facility CDI cases (7.6%) and in community acquired infections (2.3%).

7. Conclusions

There seems to be clear evidence that *C. difficile* colonisation and infection is more likely in elderly patients, as many factors associated with ageing influence susceptibility. Despite the currently limited data on the age-related changes in gut microbiota, this may play a critical role in *C. difficile* colonisation. Antibiotics, as well as specific treatments or interventions, and other individual conditions that decrease immune defences appear to promote the development of infection.

Hospitals are traditionally considered to be the main focus of *C. difficile* contamination, but some studies have also highlighted long-term care facilities as an environment predisposed for transmission. The constant movement of patients from nursing homes to hospitals and vice versa may facilitate transmission of epidemic and non-epidemic *C. difficile* strains between both of the healthcare establishments.

The severity and mortality rate of CDI appears more elevated among nursing home residents than older people living in the community. In addition, the hypervirulent PCR-ribotype 027 have been described as the most prevalent strain in long-term care facilities for elderly people.

Although it is difficult to separate the increased CDI susceptibility of nursing home residents from that induced by other factors (e.g. exposure to antibiotics, hospitalisation), further studies are required to better understand the epidemiology of *C. difficile* in long-term care facilities, in both the presence and absence of an epidemic situation.

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