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Diarrhea, *Clostridium difficile*, and Intestinal Inflammation in Residents of a Long-Term Care Facility

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Abstract

Introduction—Long-term care facilities (LTCF) residents have been estimated to have the highest incidence of diarrheal illness among adults living in the developed world. This study describes undiagnosed diarrhea, intestinal inflammation, and *Clostridium difficile* colonization in a LTC population and explores whether these are associated with functional decline, as defined by weight loss or a change in cognitive or ADL status.

Methods—An observational study of a convenience sampling of residents in a 180-bed LTCF was obtained; evaluation of stool and medical records was done. Stool specimens were evaluated for consistency, gross blood, inflammation (via quantitative fecal lactoferrin, IBD-SCAN), and *C difficile* (via PCR for gdh). SPSS and STATA were used and significance was set at $P < .05$.

Results—There were 46 stools collected; 13 of the subjects were male, 28 were older than 65 years, and 35 were prescribed 5 to 15 medications. Twenty-six of the 46 stools collected had elevated quantitative fecal lactoferrin levels. Although only 5 subjects were reported to have diarrhea (4 with elevated lactoferrin), 28 stool specimens were observed to be liquid or semi-solid (19 with elevated lactoferrin), and these liquid/semisolid stools were significantly correlated with lactoferrin positivity ($P = .017$). In analysis of functional status, there was no statistically significant association between change in ADL (n = 17) or cognitive status (n = 5) and elevated lactoferrin. However, all 3 subjects who had significant weight loss had elevated lactoferrin, although the mean fecal lactoferrin was not statistically different from those without weight loss. Of the 2 samples with *C difficile*, both were liquid and, when compared with all other liquid stools (n = 22), the mean lactoferrin was statistically higher (134.1 versus 28.8 μg/mL, $P = .008$). These 2 subjects had neither weight loss nor change in cognitive status, but 1 had a change in ADL status.

Discussion and conclusions—Diarrhea in LTCF residents is underdiagnosed. Diarrhea and the presence of *C difficile* in the stool are associated with intestinal inflammation, as detected by fecal lactoferrin. With our small numbers, we were not able to identify a specific link; however, we were able to identify a correlation between weight loss and intestinal inflammation, but, with just 2

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samples, not *C difficile* colonization. This relationship highlights the importance of larger studies to further examine the rate of diarrhea in LTCF; the effect of diarrhea and intestinal inflammation on weight loss; and the interaction of *C difficile* colonization with weight loss, malnutrition, and functional decline.

Keywords

Diarrhea; long-term care; Clostridium difficile; functional decline; fecal lactoferrin

Diarrhea is major cause of illness among residents of long-term care facilities (LTCF) and skilled nursing facilities. In 1993, Bennett and Greenough[1] reported that "perhaps the most important risk factor for developing diarrhea for an older person is whether that individual resides in a nursing home. Among adults in the developed world, residents of nursing homes, no doubt, have the highest incidence of diarrheal illness." A report of deaths from diarrheal illnesses from 1979 to 1987 found that 51% of mortalities occurred in those older than 74 years. 2 There are many causes of diarrhea in the LTC setting; however, the most common infectious cause of nonepidemic acute diarrhea in LTC is *Clostridium difficile*.[3,4] There are multiple population factors that contribute to these high rates, including the following:

- Transfers between the LTCF and acute care hospitals introduce *C difficile* and other enteric pathogens into the environment on a continuous basis
- Large numbers of medically frail residents with incontinence and cognitive disorders
- Close quarters
- Social interactions are encouraged
- Antibiotic use is frequent
- Staff–patient ratios are high
- Infection control resources are few[5]

C difficile is a major cause of nosocomial diarrhea, but the full and distinct impact on LTCF residents is not fully understood. Internationally, there have been multiple recent reports of an increase in the number and severity of *C difficile* infections,[6–8] hospitalizations,[9] and *C difficile*–related mortality.[10] Locally, we have found that the number of cases of *C difficile* has steadily increased since 2002 for hospitalized patients.

Although risk factors for *C difficile* infection in LTCF are similar to those for patients in acute care settings, immuno-compromised and elderly patients have always been at increased risk for *C difficile* infection. This perhaps reflects a frail population that can acquire *C difficile* from their environment and, in the setting of waning immunity and antibiotic use, develop symptomatic infection.[5]

Studies that have attempted to evaluate the prevalence of *C difficile* in LTCF have varied greatly in rates, methodology, and risk-factor analyses. Nonetheless, in nonepidemic settings,

- Point prevalence surveys detected rates of 1.8% and 7.7%, based on positive culture or toxin assays, in a chronic care facility for older adults.[11] Although many of these patients had been hospitalized previously, antibiotic use was not found to be a risk factor.
- In a larger study, 70% of chronic-care ward patients and 26% of nursing home residents (overall 33% of the LTCF residents) had *C difficile* in their stool within 2 weeks of antibiotic treatment, but most did not have symptoms of diarrhea.[12]

- Numerous studies from 1980s and 1990s have reported the prevalence of asymptomatic carriage among LTCF residents from 4% to 20%.[3,11,13–20]

C difficile infection in the elderly has also been shown to cause a protein-losing enteropathy, which increases the risk for malnutrition in an already vulnerable population.[21] We evaluated the strains of *C difficile* present in local residents of a LTCF and to analyze the strain-specific effects of infection on mortality, nutritional status (diarrhea, weight loss, malnutrition), and quality of life/functional status. This is a pilot study to look at an asymptomatic LTCF population and determine if undiagnosed diarrhea, intestinal inflammation, and colonization can be associated with functional decline; specifically weight loss, change in activities of daily living (ADL), and change in cognitive status.

METHODS

Institutional review board exemption for this study was obtained because the data analyzed by the research group was de-identified. An observational study of a convenience sampling of residents in a 180-bed LTCF was done; 46 stool samples were collected and the medical records of those residents were evaluated. Stools were evaluated for consistency, gross blood, inflammation (via IBD Scan ELISA (TechLab, Inc.) for quantitative fecal lactoferrin), and *C difficile* (via polymerase chain reaction [PCR] for *gdh* (glutamate dehydrogenase, a *C. difficile* housekeeping gene) and *tcdB* (gene that encodes for *C. difficile* toxin B)). To be classified as having diarrhea, a subject would either be noted on the Minimum Data Set (MDS) to have diarrhea on “Bowel Elimination Pattern” (item H2) or the subject ’s stool specimen took the shape of the container, having liquid or semi-solid stool. Review of the medical record included the most recent MDS available for each resident and a review of the medical chart was done by the facility staff. MDS item B6 was used to evaluate for recent change in cognitive status. The statement of B6 is as follows:

Resident ’s cognitive status, skills, or abilities have changed as compared to status of 90 days ago (or since last assessment if less than 90 days) had the possible replies as follows:

A. No change

B. Improved

C. Deteriorated.[22]

Only subjects noted to have deteriorated cognitive status via MDS were categorized as having a change in cognitive status for study purpose. Similarly, item G9 was used to evaluate for change in ADL function, with identical categorizations. SPSS (SPSS, Inc., Chicago, IL) and STATA (StataCorp LP, College Station, TX) were used for analysis and significance was set at P less than .05.

RESULTS

See Table 1 for detailed demographics. Of the 46 residents investigated, only 5 were reported to have diarrhea via MDS. Of those 5 samples, 4 were positive for quantitative fecal lactoferrin. However, on examination of the samples, 28 stools were liquid or semi-solid and 19 of these samples were positive for quantitative fecal lactoferrin (see Figure 1).

Liquid/semisolid stools were significantly correlated with positive quantitative fecal lactoferrin (P = .017). Of the 46 stools collected, 26 had elevated quantitative fecal lactoferrin levels. See Figure 2 for details of mean values of quantitative fecal lactoferrin and Table 2 for detailed lactoferrin levels by subset of our population. There was no statistically significant association between change in ADL (n = 17) or cognitive status (n = 5) and quantitative fecal lactoferrin levels. However, each of the 3 subjects who had significant weight loss had elevated

quantitative fecal lactoferrin levels, although mean lactoferrin level was not statistically different from those without weight loss. Of the 2 samples with *C difficile*, both were liquid and, when compared with all other liquid stools (n = 22), the mean lactoferrin was statistically higher (134.1 versus 28.8 μg/mL, P = .008). Each of the 2 samples that were positive for *gdh* were negative for toxin B (via *tcdB*). See Table 3 for details.

DISCUSSION

One of the limitations of this study is the level of detail available from the MDS data. All data were recorded for clinical purposes and not for this research study. Changes in cognitive status and ADL function were based on a subjective assessment by LTCF staff and not further characterized in the MDS. Residents who had functional or cognitive changes, but had not been assessed via the MDS during the study period, would be missed. Additionally, incomplete or inaccurate reporting of changes in cognitive status and ADL function on the MDS also limits this study. Given the underrepresentation of diarrhea on the MDS, it may correlate that changes in ADL and/or cognitive status were also under-represented. The ability to generalize this study is further limited by the fact that this was a convenience sampling of residents of a single facility during a nonepidemic time.

This study finds that diarrhea is underdiagnosed in our LTCF. Of the patients who were found to have diarrhea, 26% had elevated quantitative fecal lactoferrin, as a marker of intestinal inflammation. This could skew our results that patients with multiple stools may have been more likely to have a stool sample submitted. However, because of the limited scope of this project, we were unable to obtain a stool specimen from every resident in the facility. Such studies will be important to define the frequency, causes, and impact of diarrhea and intestinal inflammation in the elderly.

CONCLUSIONS

Diarrhea in LTCF residents is underdiagnosed. Diarrhea is a major cause of morbidity and mortality for children and the elderly. In 1992, Gangarosa et al[23] evaluated the case-fatality rate for diarrhea. They found that, “while children aged less than 5 years and adults aged 60 years or more each comprised one fourth of hospitalizations involving gastroenteritis, the older group represented 85% of diarrheal deaths. Age was the most important risk factor for death subsequent to a hospitalization involving gastroenteritis (odds ratio = 52.6, 95% confidence interval 37.0–76.9 for age greater than or equal to 70 years vs. less than 5 years).” In the May 2009 issue of this *Journal*, in an article entitled “Diarrhea in Long-Term Care: A Messy Problem,” Drs. Morley and Steinberg[24] describe that “diarrhea is a major and often under-recognized problem in long-term care. It is a major cause of morbidity (especially weight loss, dehydration, and delirium) and mortality, as well as being costly.” Our study reemphasizes that in our facility, diarrhea was a substantially underdiagnosed problem.

In this study, diarrhea, even without *C difficile* in the stool, was associated with intestinal inflammation, as detected by fecal lactoferrin. This suggests that the diarrhea seen in this study was not medication or diet related, but reflected an underlying inflammatory pathology. Despite the small sample size, we are able to identify a correlation between weight loss and intestinal inflammation; although with our small numbers, not *C difficile* colonization. This relationship highlights the importance of examining further the rate of diarrhea in LTCF; the effect of diarrhea and intestinal inflammation on weight loss; and the interaction of *C difficile* colonization with weight loss, malnutrition, and functional decline.

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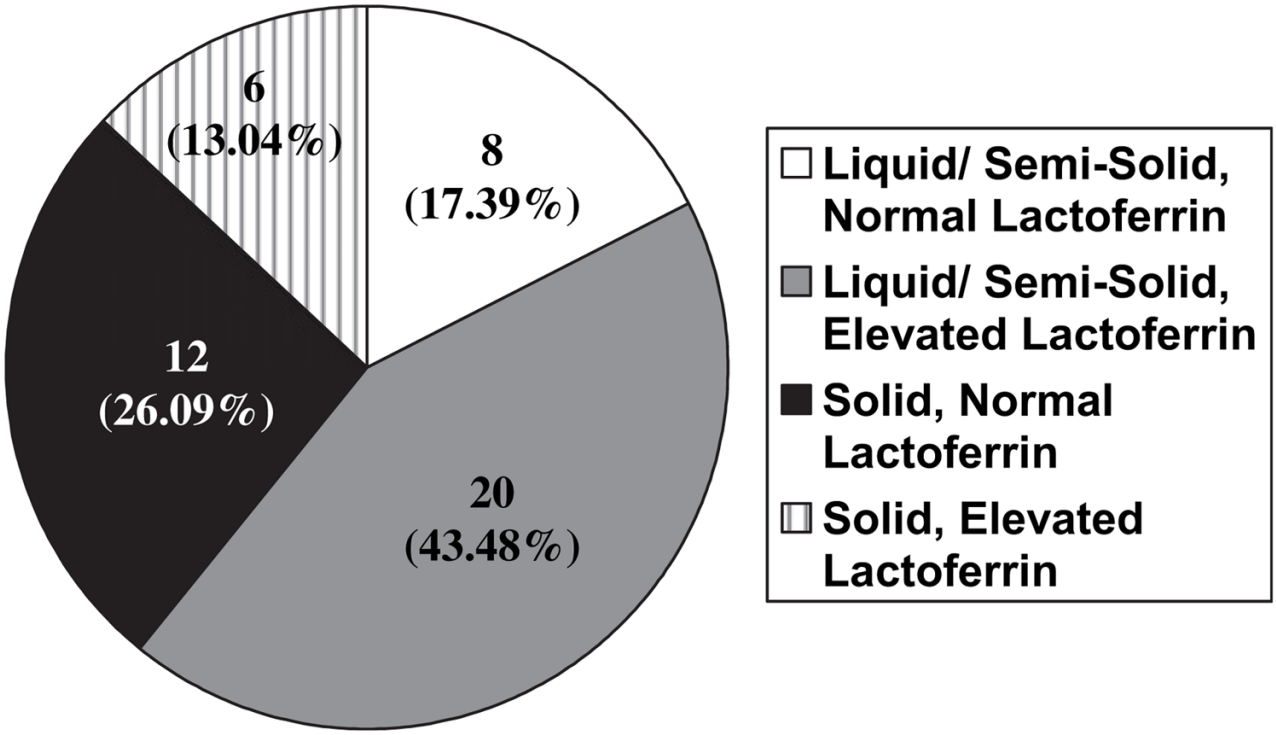
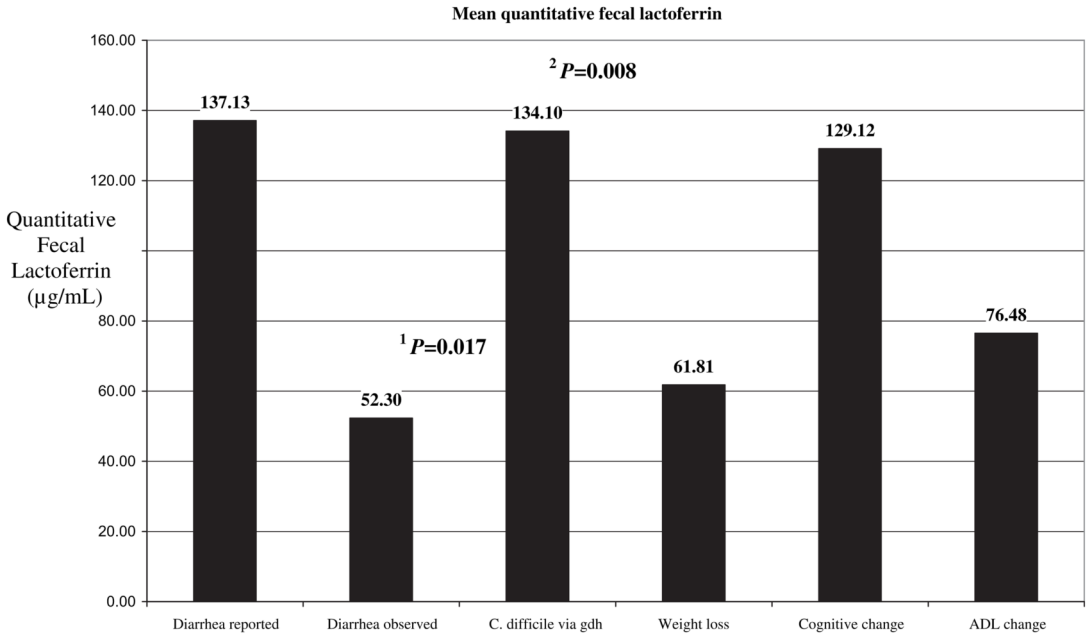


Fig. 1.
Stool consistency and quantitative fecal lactoferrin status.



[1] Analysis of fecal lactoferrin level for all liquid/ semi-solid stools, as compared to all solid stools.

[2] Analysis of fecal lactoferrin level for stools testing positive for *gdh* via PCR as a marker for *C. difficile*, as compared to all liquid/ semi-solid stools.

Fig. 2.
Mean levels of quantitative fecal lactoferrin.

Table 1

Available Demographics (N = 46)

Gender	34 Female
Age	28 ≥ 65 years old
No. of medications	35 prescribed 5–15 medications
	11 prescribed >15 medications

Table 2

Quantitative Fecal Lactoferrin for Each Subset Population

	Diarrhea Reported	Diarrhea Observed	*Clostridium difficile* via PCR for *gdh*	Weight Loss	Cognitive Change	ADL Change
No. of samples total	5	28	2	3	5	17
No. of samples with elevated fecal lactoferrin	3	19	2	3	2	10
Minimum level fecal lactoferrin (μg/mL)	137.13	10.2	14.29	13.78	99.37	11.41
Mean level fecal lactoferrin (μg/mL)	14.00	52.3	134.10	61.87	129.12	76.48
Maximum level fecal lactoferrin (μg/mL)	253.00	254.00	253.95	152.76	158.86	253.95

ADL, activity of daily living; PCR, polymerase chain reaction.

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Table 3

Description of Subjects with Weight Loss and C difficile in Stool

Subjects with *C difficile* (n = 2)
Age < 65 years old and 85 years old
Male and female
9 and 8 medications prescribed
Housed on different wards
Both had liquid stools
1 had change in ADL status
Neither had weight loss or cognitive change
Statistically higher fecal lactoferrin than all other subjects (134.1 versus 28.8 μg/mL; P =.008)

ADL, activity of daily living.