Dietary Calcium and Risk of Microscopic Colitis

Robert S. Sandler, MD, MPH[1,2], Shan Sun, PhD[1], Temitope O. Keku, PhD[1,2], John T. Woosley, MD, PhD[3], Chelsea Anderson, PhD[1], Anne F. Peery, MD, MSCR[1,2] and Anthony Fodor, PhD[4]

BACKGROUND: **Microscopic colitis (MC) is an increasingly common cause of watery diarrhea particularly in older individuals. The role of diet in MC has received little study.**

METHODS: **We conducted a case-control study at a single institution enrolling patients referred for elective outpatient colonoscopy for diarrhea. Patients were classified as cases with MC or non-MC controls after a review of colon biopsies by 1 research pathologist. Study subjects were interviewed by a trained telephone interviewer using a validated food frequency questionnaire. Adherent microbes were evaluated from colonic biopsies using 16s rRNA sequencing.**

RESULTS: **The study population included 106 cases with MC and 215 controls. Compared with controls, the cases were older, better educated, and more likely to be female. Cases with MC had lower body mass index and were more likely to have lost weight. Subjects in the highest quartile of dietary calcium intake had a lower risk of MC compared with those in the lowest quartile (adjusted odds ratio 0.22, 95% confidence interval 0.07–0.76). The findings were not explained by dairy intake, body mass index, or weight loss. We found that dietary calcium intake had significant associations with the abundance of Actinobacteria and Coriobacteriales in the microbial community of colonic biopsies.**

DISCUSSION: **Compared with patients with diarrhea, cases with MC had a lower intake of dietary calcium. Diet can be associated with alterations in the gut microbiota and with luminal factors that could affect the risk of MC.**

KEY WORDS: case-control; colitis; epidemiology; microbiome

SUPPLEMENTARY MATERIAL accompanies this paper at http://links.lww.com/CTG/A912

Clinical and Translational Gastroenterology 2023;14:e00569. https://doi.org/10.14309/ctg.0000000000000569

INTRODUCTION

Microscopic colitis (MC) is a common cause of chronic watery diarrhea. The mucosa appears endoscopically normal or nearly normal (1). Microscopically, however, there is a thickened collagen band (collagenous colitis) or lymphocytic infiltration (lymphocytic colitis) (2). Published incidence and prevalence figures vary widely. The pooled overall incidence from studies providing population-based data was 11.4 (95% confidence interval [CI] 9.2–13.6) per 100,000 person-years. The pooled prevalence was 119 (95% CI 73–166) (3). The disease has an important impact on quality of life (4,5). Patients with MC describe isolation and withdrawal from social life and activities (6).

It is common to examine diet in chronic digestive diseases to find clues to etiology. Such inquiry makes sense because dietary constituents come in direct contact with digestive organs. Diet can affect the gastrointestinal tract directly or indirectly by promoting or inhibiting the growth of microorganisms. There have been many published article on diet and inflammatory bowel disease (Crohn's disease and ulcerative colitis) (7). Surprisingly, diet has rarely been studied as a risk factor of MC (8,9).

To bridge the gap in our understanding of the role of diet in MC, we conducted a case-control study that included detailed questions about diet. All the subjects—cases and controls—were referred for colonoscopy because of chronic diarrhea, thereby reducing the risk of biased recall. We obtained mucosal biopsies to evaluate the possible role of the microbiome in conjunction with diet.

MATERIALS AND METHODS

Design

The study included patients who were referred to The University of North Carolina Hospitals between April 1, 2015, and December 22, 2020, for elective outpatient colonoscopy for diarrhea. Based on a chart review, patients were excluded if the indication

[1]Center for Gastrointestinal Biology and Disease, Chapel Hill, North Carolina, USA; [2]Department of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA; [3]Department of Pathology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA; [4]Department of Bioinformatics and Genomics, University of North Carolina at Charlotte, Charlotte, North Carolina, USA.
Correspondence: Robert S. Sandler, MD, MPH. E-mail: rsandler@med.unc.edu.
Received December 15, 2022; accepted February 13, 2023; published online February 24, 2023

for colonoscopy was neither diarrhea or possible MC or if they had a diagnosis of inflammatory bowel disease, *Clostridium difficile* or another infectious diarrhea. Nominally eligible patients were sent an introductory letter and study brochure. Figure 1 describes subject eligibility, consent, interview, and pathology review for patients enrolled in the study.

Before the colonoscopy, a research assistant asked patients the average number of bowel movements per day and stool form based on the Bristol Stool Form Scale (10). To be eligible, the patient had to report a Bristol Stool Form type 5, 6, or 7 (mushy, loose, and watery, respectively) during the week before colonoscopy regardless of the number of bowel movements. All participants provided written informed consent. Blood was drawn and stored for consented patients.

Colonoscopies were performed by faculty gastroenterologists and supervised fellows. If the colonoscopy revealed gross inflammation (ulceration and erosions), the patient was excluded. Clinical biopsies were sent to the surgical pathology laboratory where they were reviewed by one of the faculty pathologists. If the clinical biopsies showed neutrophilic colitis or eosinophilic colitis, the patient became ineligible. If the patient was eligible, the research pathologist reviewed the slides.

There were some occasions when the research assistant was not available during the colonoscopy to consent a potentially eligible patient (Missed in Endo group in Figure 1). The telephone interviewer contacted the patient to verify eligibility and to obtain consent for the interview and the use of clinical biopsies. The research pathologist reviewed the slides to establish the pathologic diagnosis.

Some patients were not identified before colonoscopy. These were individuals with other indications for the procedure (e.g., screening) who were recognized as having diarrhea when they presented for open-access colonoscopy and had biopsies taken. To avoid missing these patients, once in each month, we used a custom query tool to identify all patients with a new pathological diagnosis of MC. If MC was found on review of the path report (MC found on path in Figure 1), patients were contacted and consented in a similar fashion as the missed group previously described. The slides were reviewed by the research pathologist. There was no age restriction for these patients.

Pathologic review

The colon biopsy slides of every subject were reviewed by 2 pathologists, a clinical pathologist and the research pathologist (J.T.W.). In instances where the 2 pathologists disagreed, the slides were read for a second time by the research pathologist. The subject was classified as having MC or not (the controls) based on the final reading of the research pathologist. The pathologist was

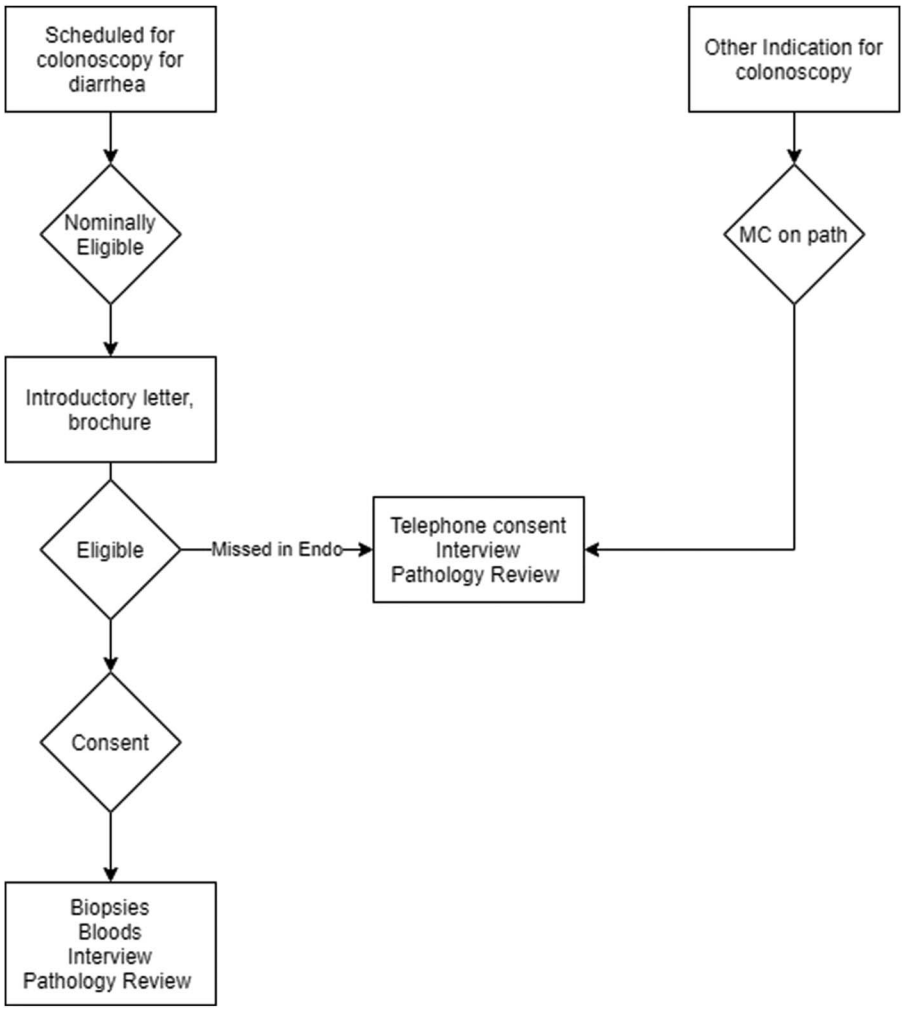

Figure 1. Eligibility, consent, interview, and pathology review for patients enrolled in the study. MC, microscopic colitis.

Table 1. Characteristics of the study population

	Case (N = 106)		Control (N = 215)		
	No.	%	No.	%	*P* value
Age, mean (SD)	63.2	12.7	54.7	11.8	<0.001
Race					0.009
White	102	96	185	87	
Non-White	4	4	28	13	
Sex					0.005
Female	91	86	154	72	
Male	15	14	61	28	
Marital status					0.44
Married	75	71	143	67	
Not married	31	29	72	33	
Education					<0.001
Less than college	36	34	119	55	
College or postgraduation	70	66	96	45	
Cigarette smoking					0.03
Yes	12	11	45	21	
No	94	89	170	79	
BMI, mean (SD)	25.6	6.5	29.5	7.1	<0.001

BMI, body mass index.

not aware of patient symptoms or diagnosis. When the research pathologist noted patchy lymphocytes, the diagnosis was categorized as "indeterminate MC." For this analysis, we excluded indeterminate cases. There were too few indeterminate cases (14) for a separate analysis and including them in either the MC case group or the control group would lead to misclassification.

Interviews

Patients were given the option to complete the interview using a web-based survey or phone interview. Those who indicated an interest in the web-based survey were sent a personalized link with reminders on days 5, 10, and 13. Those who had not completed the survey in 20 days were called by the telephone interviewer to complete the interview. The questions and response options for the web-based survey and the telephone interview were identical. The major sections of the questionnaire were as follows: demographics, smoking, medical history, medications taken in the last year, reproductive history (women), MC disease activity, and irritable bowel and bloating questions (Rome Foundation–licensed agreement with Rome Foundation October 24, 2017). For medications, we asked patients how many weeks they took the medication during the year before their colonoscopy. The requirement that all patients have diarrhea was designed to reduce recall bias. If cases had diarrhea but not controls, the cases might have differential recall of past diet or other exposures.

Diet survey

We used the Dietary Screener Questionnaire (DSQ) developed at the National Cancer Institute (11). The DSQ records information on dietary intake over the past year to account for seasonal changes. The DSQ was developed in a population of 7,588 individuals who participated in the National Health and Nutrition Examination Survey study. The questions have been cognitively tested and have been validated. Analysis software from the National Cancer Institute generates summary data on average daily intake of fiber, calcium, whole grains, sugar, dairy, fruits and vegetables combined or separately, and sugar from sugar-sweetened beverages. For this analysis, we excluded participants missing all dietary intake variables (n = 4 cases, n = 37 controls).

Data analysis

Characteristics were compared between cases and controls using χ^2 tests for categorical variables and *t* tests for continuous variables. In analyses stratified by sex, we calculated the median daily dietary intake according to case-control status. *P* values comparing dietary intake between cases and controls were estimated using Wilcoxon rank sum tests. To examine the association between diet and MC, we estimated odds ratios and 95% CIs according to quartiles of dietary intake variables. Quartile cut points were defined using the distributions of dietary variables among controls. Multivariable models were adjusted for age, sex, body mass index (BMI), and education, characteristics that were associated with MC in unadjusted logistic regression models. We performed analyses stratified by reported weight loss (any vs none) since the onset of diarrhea. Missing data were not imputed. Analyses were conducted using SAS software, version 9.4 (Cary, NC).

Microbiome analysis

DNA extraction, poymerase chain reaction and sequencing methods, and analysis of sequences have been described in a previous publication (12). In brief, DNA was extracted from ascending and descending colon biopsies. The bacterial 16S rRNA gene V2 region was amplified with poymerase chain reaction and

Table 2. Median and Interquartile range (IQR) daily dietary intake for cases and controls stratified by sex

Dietary variable (per d)	Women					Men				
	Case (n = 91)		Control (n = 154)			Case (n = 15)		Control (n = 61)		
	Median	IQR	Median	IQR	*P* Value	Median	IQR	Median	IQR	*P* Value
Fiber (g)	14.21	12.91–16.32	14.02	12.43–15.40	0.31	16.68	15.45–18.94	18.15	15.27–21.08	0.22
Calcium (mg)	807.23	733.94–877.38	800.27	732.25–888.93	0.98	957.10	904.43–1,075.25	1,055.03	989.83–1,199.59	0.08
Whole grain (oz.)	0.54	0.42–0.86	0.53	0.39–0.75	0.43	0.48	0.33–0.88	0.66	0.37–1.17	0.37
Sugar (tsp.)	12.46	11.15–14.77	13.50	11.57–17.36	0.01	15.92	11.74–19.00	15.30	12.24–21.84	0.84
Dairy (cups)	1.22	1.04–1.40	1.24	1.07–1.47	0.43	1.42	1.13–1.77	1.60	1.30–1.92	0.19
Fruit/veg (cups)	2.19	1.96–2.50	2.20	1.97–2.54	0.75	2.65	2.21–2.75	2.60	2.22–3.47	0.46
Vegetables (cups)	1.32	1.22–1.44	1.31	1.21–1.45	0.87	1.59	1.55–1.75	1.64	1.44–1.88	0.75
Fruit (cups)	0.82	0.64–1.00	0.77	0.57–0.98	0.27	0.90	0.52–1.00	0.81	0.59–1.43	0.39
Added sugar from sugar-sweetened beverages (tsp equivalents)	3.58	3.57–4.33	4.42	3.71–6.91	<0.001	6.84	4.58–8.57	5.53	4.65–9.03	0.97

sequenced on an Illumina Miseq platform. The sequences were analyzed with Divisive Amplicon Denoising Algorithm and Quantitative Insights Into Microbial Ecology to characterize the microbial communities of the biopsies. Patients who took antibiotics were excluded for the microbiome analysis. We analyzed the associations between microbiome and calcium consumption of patients with the Kendall correlation. *P* values were adjusted with the Benjamini-Hochberg method to correct for multiple hypothesis testing. Rare taxa (presence in <75% samples) were not included in the analysis.

Informed consent

The study was approved by the Institutional Review Board at the University of North Carolina. All patients gave informed consent. All authors had access to the study data and reviewed and approved the final manuscript.

RESULTS

The study population consisted of 106 cases with MC and 215 controls. The 2 subtypes of MC (collagenous colitis and lymphocytic colitis) were combined in this analysis to improve study power. As summarized in Table 1, the cases were almost a decade older, on average, than the controls. Most of them were White, including 96% of the cases and 87% of controls. Cases were more likely to be women when compared with controls, 86% vs 72%. The overall population was well educated. A higher proportion of the cases had college or postgraduate education (66%) than controls (45%). More controls smoked cigarettes. The BMI of the controls was greater than that of the cases.

Crude dietary intake by case-control status, stratified by sex, is summarized in Table 2. Because men are generally larger than women and require more calories, we stratified by sex to explore potential effect measure modification. Among women, cases ate less total sugar and added sugar from sugar-sweetened beverages than controls.

Table 3 examines odds ratios for MC according to quartiles of consumption. Compared with the lowest quartile, individuals in the highest quartile of dietary calcium intake had a lower risk of MC, adjusted odds ratio 0.22, 95% CI 0.07–0.76, after adjusting for age, education, BMI, and sex. The finding was not explained by consumption of dairy products. The results were unchanged in an analysis controlling for dairy consumption or in analyses stratified by dairy consumption.

Cases consumed less sugar from sugar-sweetened beverages than controls (median = 3.67 vs 4.93 tsp. equivalents for men and women combined). Because patients with MC were more likely to lose weight, we examined whether weight loss explained the difference in the consumption of sugar from sweetened beverages. When we stratified by whether the subject lost weight, there was no association in the subgroup with no weight loss. Among the group that lost weight, however, there was a lower risk of MC associated with sugar-sweetened beverages with wide CIs (see Supplementary Table 1, http://links.lww.com/CTG/A912).

We previously reported that there are taxa associated with MC in colon biopsy microbial communities (12). To understand whether any gut microbe plays a role in the association between calcium consumption and risk of MC, we analyzed the correlations between calcium consumption and the abundance of microbes in the microbial community. We found that the abundance of phylum Actinobacteria and order Coriobacteriales in both the ascending and descending colon were significantly positively correlated with calcium consumption (Figure 2). The order Coriobacteriales belongs to

Table 3. Risk of microscopic colitis by quartile of dietary consumption (odds ratios and 95% CI)

	Quartile of consumption			
Dietary variable (per d)	1	2	3	4
Fiber (g)	Ref	0.71 (0.32–1.58)	0.74 (0.33–1.69)	0.65 (0.26–1.63)
Calcium (mg)	Ref	1.19 (0.55–2.59)	0.99 (0.43–2.27)	0.22 (0.07–0.76)
Whole grain (oz.)	Ref	1.29 (0.58–2.87)	0.80 (0.33–1.92)	1.14 (0.51–2.54)
Sugar (tsp.)	Ref	0.68 (0.32–1.46)	0.82 (0.40–1.67)	0.66 (0.28–1.57)
Dairy (cups)	Ref	1.08 (0.52–2.26)	0.89 (0.42–1.89)	0.64 (0.27–1.54)
Fruit/veg (cups)	Ref	1.07 (0.49–2.33)	0.80 (0.35–1.80)	0.84 (0.36–2.00)
Vegetables (cups)	Ref	1.66 (0.78–3.54)	1.47 (0.67–3.23)	1.04 (0.41–2.66)
Fruit (cups)	Ref	0.75 (0.33–1.71)	0.73 (0.32–1.65)	0.73 (0.31–1.71)
Sugar-sweetened beverages	Ref	0.45 (0.21–0.97)	0.33 (0.13–0.84)	0.78 (0.33–1.83)

Adjusted for age, sex, education, and BMI.
BMI, body mass index; CI, confidence interval.

phylum Actinobacteria and likely contributed to the abundance changes of Actinobacteria. Coriobacteriales was the only order belonging to class Coriobacteriia in this data set, so Coriobacteriia have the same abundance change and significant correlations with dietary calcium as Coriobacteriales. Thus, we did not include Coriobacteriia in the figure.

DISCUSSION

MC is a sometimes-debilitating disease that most often affects older patients, particularly women. Although the etiology of MC unknown, fecal constituents have been strongly implicated. MC goes into remission when the fecal stream is diverted and recurs when continuity is restored (13). Based on the effects of fecal diversion, diet is certainly worth scrutiny. Dietary elements that are not absorbed appear in the colon, and diet can influence the colonic microbiome. In this study, we examined dietary exposures in a well-characterized group of patients. The data showed, intriguingly, that dietary calcium had a protective association. There was an association between calcium intake and Actinobacteria, raising the possibility that the effect of calcium could be mediated by the microbiome.

The association between diet and MC has been examined in a population-based study from Malmo (9). The study included 135 patients who were diagnosed with MC over a 22-year period. There was no association with MC for the intake of protein, carbohydrates, sucrose, saturated fat, monounsaturated fat, polyunsaturated fat, omega-3 or omega-6 fatty acids, fiber, and zinc. There was an association with alcohol. We did not ask about alcohol in this study.

There is only 1 prior US study that has examine diet in MC. That study did not report on diet but did report on alcohol. Niccum et al (14) found an association with alcohol in 2 large cohorts of nurses. The study included 352 incident cases of MC with nearly 5 million person-years of follow-up. A higher alcohol consumption was associated with an increased risk of MC. Compared with nonusers, the adjusted hazard ratios were 1.20 (95% CI, 0.86–1.67) for 0.1–4.9 g/d of alcohol, 1.90 (95% CI, 1.34–2.71) for 5–14.9 g/d, and 2.31 (95% CI, 1.54–3.46) for of ≥ 15 g/d. Wine seemed to be a stronger risk factor than beer or liquor.

We found that individuals in the highest quartile of calcium were less likely to have MC. A study by Fuhren et al (15) reported that rats fed a diet rich in calcium phosphate favored Firmicutes and increased fecal lactic, succinic, acetic, propionic, and butyric acid levels. These short-chain fatty acids could exert a protective effect against inflammation. Conversely, they reported that relatively low dietary calcium phosphate levels promoted the abundance of mucin-degrading genera such as Akkermansia and Bacteroides, leading to higher fecal propionic acid levels and modest increases in lactic and butyric acid levels. High calcium phosphate diets increased endogenous Faecalbaculum populations when the diets were supplemented with galacto-oligosaccharides or inulin. The authors concluded that to correctly assess diet-driven microbiota analysis, it was important to collect a detailed diet information, including micronutrient balance.

A protective effect of higher calcium against MC is biologically plausible. Approximately 60% of ingested calcium appears in the colon (16). Luminal bile acids and free fatty acids have been shown to stimulate proliferation (17). Lupton et al (16) found that calcium supplementation decreased the proportion of chenodeoxycholic acid in bile and decreased the ratio of lithocholate to deoxycholate in feces. High calcium diets have also been shown to maintain intestinal integrity and regulate tight junction gene expression (18).

In our study, we found that calcium consumption was significantly correlated with the abundance of Actinobacteria, Coriobacteriia, and Coriobacteriales, suggesting that these taxa might play a role in the protective effect of dietary calcium against MC. Actinobacteria are important in maintaining gut barrier homeostasis and degradation and biotransformation of dietary substances (19). While the abundance of Actinobacteria has been reported to be related to fat, vitamin D, and fiber intake in diet (20,21), it remains unclear how different diets modify the abundance of Actinobacteria and how Actinobacteria degrades and transforms substances in diet. Thus, while a higher calcium intake increased the abundance of Actinobacteria in the gut microbiome, and Actinobacteria has been reported to be less abundant in patients with MC, the mechanism behind this association is not clear.

Medications from a number of different classes have been associated with MC (22–24). The quality of evidence supporting this association is low, as judged by the European MC Group and United

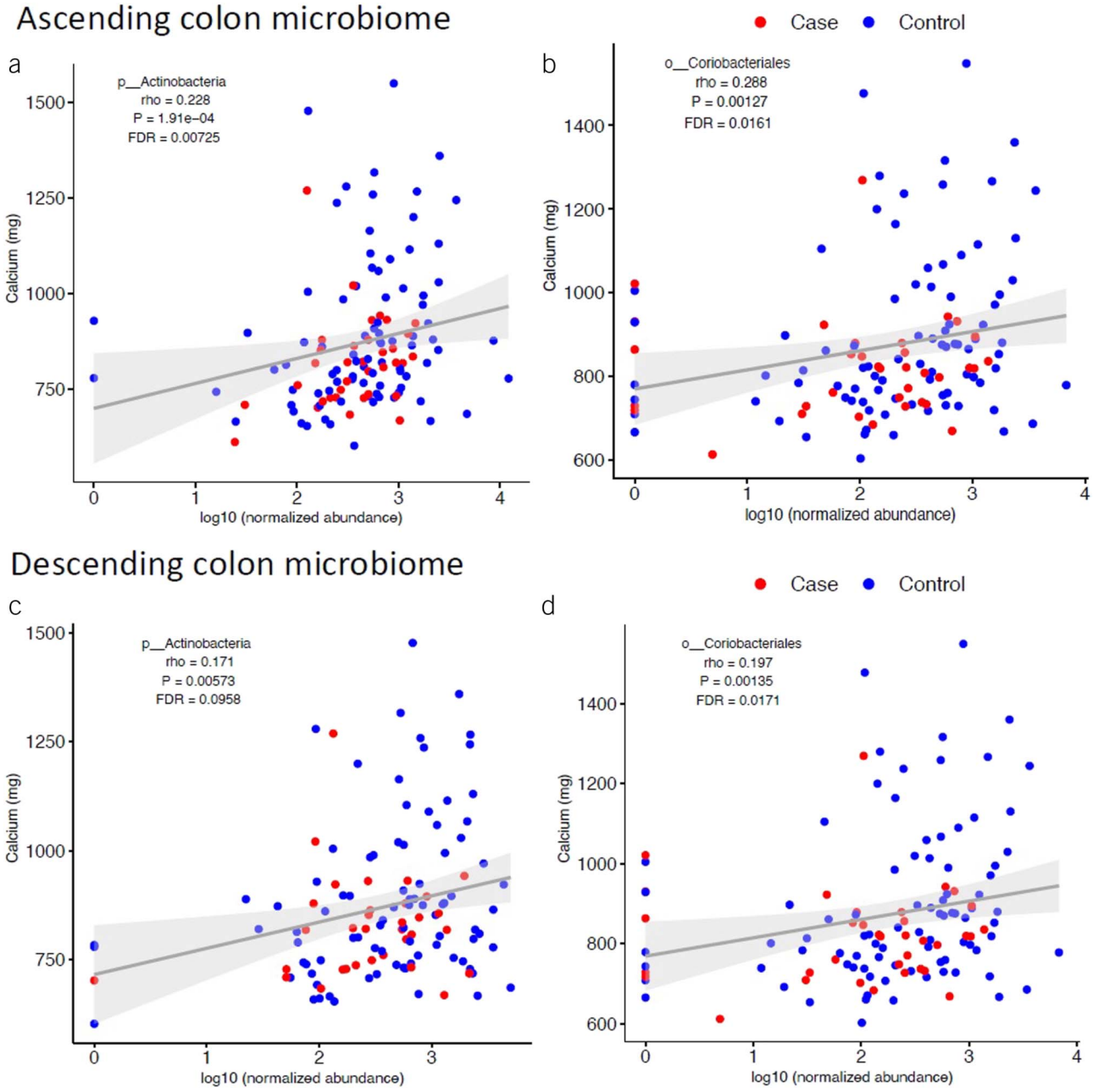

Figure 2. Microbial taxa significantly associated with calcium consumption. (**a** and **b**) In the ascending colon microbiome, the abundance of phylum Actinobacteria and order Coriobacteriales were significantly correlated with dietary calcium consumption. (**c** and **d**) In the descending colon microbiome, the abundance of phylum Actinobacteria and order Coriobacteriales were significantly correlated with dietary calcium consumption. Correlation coefficients and *P* values were calculated from the Kendall correlation. The Benjamini-Hochberg method was used to adjust for multiple hypothesis testing. Points were colored by cases (patients with microscopic colitis) and controls. The gray line represents the linear regression line across all subjects with 95% confidence interval.

European Gastroenterology (3). As previously reported, we did not find an association with medications in this study when cases were compared with controls with diarrhea (25). Similar negative studies have been reported by other studies with diarrhea controls (26–28). In the absence of an association with medications, we did not investigate interactions between diet and medications.

The strengths of this study include careful case definition, pathology review by a single experienced gastrointestinal pathologist, evaluation of diet using a validated questionnaire, and examination of adherent microbes using 16S rRNA sequencing. Because all the patients in the study underwent colonoscopy for diarrhea, factors such as symptoms, access to health care, and care-seeking behavior were comparable in cases and controls. The risk of recall bias was reduced by the fact that all patients had diarrhea. The study was limited by small sample size and lack of racial diversity. We combined lymphocytic and collagenous colitis in this study. Both forms are considered part of the same entity based on similar incidence, geographic distribution, female sex predominant, and risk factors (29). Both forms respond similarly to treatment with budesonide.

The key to understanding the etiology of MC is determining the factors in the colonic lumen that are responsible. We found that dietary calcium intake, possibly mediated by specific bacteria, was associated with risk of MC. These intriguing findings can help direct future mechanistic studies.

CONFLICTS OF INTEREST

Guarantor of the article: Robert S. Sandler, MD, MPH.

Specific author contributions: R.S.S.: study concept and design, acquisition of data, analysis and interpretation, drafting manuscript, critical revisions, statistical analysis, and obtaining funding. C.A.: analysis and interpretation, critical revisions. T.O.K.: study concept and design, acquisition of data, analysis and interpretation, critical revision, AF analysis and interpretation, critical revisions, statistical analysis, and obtaining funding. A.F.P.: analysis and interpretation, critical revisions, and statistical analysis. S.S.: analysis and interpretation, critical revisions, and statistical analysis. J.T.W.: study concept and design, acquisition of data, analysis and interpretation, and critical revisions. All the authors approved the final draft submitted.

Financial support: This research was supported partly by grants from the National Institutes of Health (P30 DK034987, R01 DK105114).

Potential competing interests: None to report.

Study Highlights

WHAT IS KNOWN

- ✓ Luminal factors are important in microscopic colitis based on improvement with fecal diversion.
- ✓ Diet has rarely been studied.

WHAT IS NEW HERE

- ✓ Increased dietary calcium was associated with a lower risk of microscopic colitis and with Actinobacteria and Coriobacteriales.
- ✓ The associations with diet and microbes may explain the beneficial effects of fecal diversion and motivate further research.

REFERENCES

1. Marlicz W, Skonieczna-Zydecka K, Yung DE, et al. Endoscopic findings and colonic perforation in microscopic colitis: A systematic review. Dig Liver Dis 2017;49(10):1073–85.
2. Robert ME. Microscopic colitis. J Clin Gastroenterol 2004;38(Suppl 1): S18–S26.
3. Miehlke S, Guagnozzi D, Zabana Y, et al. European guidelines on microscopic colitis: United European Gastroenterology and European Microscopic Colitis Group statements and recommendations. United Eur Gastroenterol J 2021;9(1):13–37.
4. Munch A, Aust D, Bohr J, et al. Microscopic colitis: Current status, present and future challenges. J Crohns Colitis 2012;6(9):932–45.
5. Hjortswang H, Tysk C, Bohr J, et al. Health-related quality of life is impaired in active collagenous colitis. Dig Liver Dis 2011;43(2):102–9.
6. Pihl Lesnovska K, Munch A, Hjortswang H. Microscopic colitis: Struggling with an invisible, disabling disease. J Clin Nurs 2019;28(19-20): 3408–15.
7. Lee D, Albenberg L, Compher C, et al. Diet in the pathogenesis and treatment of inflammatory bowel diseases. Gastroenterology 2015;148(6): 1087–106.
8. Liu PH, Lebwohl B, Burke KE, et al. Dietary gluten intake and risk of microscopic colitis among US women without celiac disease: A prospective cohort study. Am J Gastroenterol 2019;114(1):127–34.
9. Larsson JK, Sonestedt E, Ohlsson B, et al. The association between the intake of specific dietary components and lifestyle factors and microscopic colitis. Eur J Clin Nutr 2016;70(11):1309–17.
10. Lewis SJ, Heaton KW. Stool form scale as a useful guide to intestinal transit time. Scand J Gastroenterol 1997;32(9):920–4.
11. Thompson FE, Midthune D, Kahle L, et al. Development and evaluation of the national cancer institute's dietary screener questionnaire scoring algorithms. J Nutr 2017;147(6):1226–33.
12. Sun S, Blakley IC, Fodor AA, et al. Microbial associations with microscopic colitis. Clin Transl Gastroenterol 2022;13(10):e00528.
13. Jarnerot G, Tysk C, Bohr J, et al. Collagenous colitis and fecal stream diversion. Gastroenterology 1995;109(2):449–55.
14. Niccum B, Casey K, Burke K, et al. Alcohol consumption is associated with an increased risk of microscopic colitis: Results from 2 prospective US cohort studies. Inflamm Bowel Dis 2022;28(8):1151–9.
15. Fuhren J, Schwalbe M, Boekhorst J, et al. Dietary calcium phosphate strongly impacts gut microbiome changes elicited by inulin and galacto-oligosaccharides consumption. Microbiome 2021;9(1):218.
16. Lupton JR, Steinbach G, Chang WC, et al. Calcium supplementation modifies the relative amounts of bile acids in bile and affects key aspects of human colon physiology. J Nutr 1996;126(5):1421–8.
17. Govers MJ, Van der Meet R. Effects of dietary calcium and phosphate on the intestinal interactions between calcium, phosphate, fatty acids, and bile acids. Gut 1993;34(3):365–70.
18. Gomes JMG, Costa JA, Alfenas RC. Could the beneficial effects of dietary calcium on obesity and diabetes control be mediated by changes in intestinal microbiota and integrity? Br J Nutr 2015;114(11):1756–65.
19. Binda C, Lopetuso LR, Rizzatti G, et al. Actinobacteria: A relevant minority for the maintenance of gut homeostasis. Dig Liver Dis 2018; 50(5):421–8.
20. Mandal S, Godfrey KM, McDonald D, et al. Fat and vitamin intakes during pregnancy have stronger relations with a pro-inflammatory maternal microbiota than does carbohydrate intake. Microbiome 2016; 4(1):55.
21. Dominianni C, Sinha R, Goedert JJ, et al. Sex, body mass index, and dietary fiber intake influence the human gut microbiome. PLoS One 2015; 10(4):e0124599.
22. Pardi DS. Microscopic colitis. Clin Geriatr Med 2014;30(1):55–65.
23. Bonderup OK, Fenger-Gron M, Wigh T, et al. Drug exposure and risk of microscopic colitis: A nationwide Danish case-control study with 5751 cases. Inflamm Bowel Dis 2014;20(10):1702–7.
24. Masclee GMC, Coloma PM, Kuipers EJ, et al. Increased risk of microscopic colitis with use of proton pump inhibitors and non-steroidal anti-inflammatory drugs. Am J Gastroenterol 2015;110(5):749–59.
25. Sandler RS, Keku TO, Woosley JT, et al. Medication use and microscopic colitis. Aliment Pharmacol Ther 2021;54(9):1193–201.
26. Pascua MF, Kedia P, Weiner MG, et al. Microscopic colitis and medication use. Clin Med Insights Gastroenterol 2010;2010(3):11–9.
27. Guagnozzi D, Lucendo AJ, Angueira T, et al. Drug consumption and additional risk factors associated with microscopic colitis: Case-control study. Rev Esp Enferm Dig 2015;107(6):347–53.
28. Zylberberg HM, Kamboj AK, De Cuir N, et al. Medication use and microscopic colitis: A multicentre retrospective cohort study. Aliment Pharmacol Ther 2021;53(11):1209–15.
29. Rasmussen MA, Munck LK. Systematic review: Are lymphocytic colitis and collagenous colitis two subtypes of the same disease–microscopic colitis? Aliment Pharmacol Ther 2012;36(2):79–90.