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Proinflammatory diet is associated with increased risk of fecal incontinence among older women: prospective results from the Nurses' Health Study

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Fecal incontinence (FI) is a debilitating gastrointestinal (GI) disorder with a devastating impact on quality of life,[1, 2] particularly on older women partly because of unique risk factors including parity and menopause.[2, 3] Therefore, identifying modifiable factors, such as diet, are crucial for developing effective prevention strategies for FI among those at risk. We previously found higher dietary fiber intake was associated with lower FI risk,[4] providing the first population-based data to connect diet and FI prevention. However, prospective evidence on other dietary factors and FI risk has been limited. Dietary patterns may be associated with gut microbiome characteristics which may influence inflammatory responses in the GI tract[5] and drive neurosensory disturbances.[6] Moreover, chronic inflammation may drive reduced muscle mass and function,[7] and pelvic floor dysfunction is an established FI risk factor.[1, 2] We hypothesized that a proinflammatory dietary pattern may be associated with increased FI risk and tested this hypothesis in Nurses' Health Study (NHS).

We used prospective data from NHS, an ongoing US cohort started in 1976.[8] Every two to four years, participants complete follow-up questionnaires and update their lifestyle and health information. Our current analysis included 57,432 participants with completed dietary data who reported no prevalent FI on the 2008 questionnaire. Participants with histories of inflammatory bowel disease, colorectal cancer and/or inability to walk were excluded. Incident FI was defined as a report of at least one liquid or solid FI episode per month in the past year on the 2010 or 2012 questionnaires; weekly FI episodes denoted severe FI.

Proinflammatory dietary pattern was quantified by the energy-adjusted Empirical Dietary Inflammatory Pattern (EDIP) Score, a previously-validated, weighted sum of 18 food groups most predictive of three established plasma inflammatory markers: C-reactive protein, interleukin-6, and tumor necrosis factor alpha-receptor 2.[9] Higher scores indicate more proinflammatory diets while lower scores indicate anti-inflammatory diets.

We used Cox proportional hazards regression models to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between recent EDIP (2006, updated through 2010) and FI risk. Three models were built: 1). Model 1: Cox models stratified by age and time period; 2). Model 2: Covariates included in model 1 + race, smoking status, body mass index, physical activity, menopausal hormone use, parity, history of hypertension, diabetes, neurologic disease, hysterectomy, and cholecystectomy; 3). Model 3: Covariates included in model 2 + dietary fiber intake. Potential effect modification by above-listed covariables on the EDIP-FI relationship were assessed by including a cross-product term of EDIP quintiles and each variable in Model 3; significance of the interaction term was evaluated by Wald tests. To demonstrate the robustness of our findings, two secondary analyses were performed: 1). Using severe weekly FI as outcome; 2). Using long-term pro-inflammatory diet captured by cumulative average EDIP (1984-2010) score as the exposure. Analyses were performed using SAS (Unix 9.4). Detailed descriptions of methods can be found in the Supplementary Methods.

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Baseline participant characteristics according to EDIP quintiles are presented in Table S1. Among 57,432 participants, 6,896 FI cases were identified over 190,000 person-years of follow-up. Proinflammatory diet was significantly associated with increased FI risk. Compared to the lowest quintile of recent EDIP, women in the highest quintile had 17%, 26%, and 19% increased risk of overall FI [HR (95% CI) = 1.17 (1.08, 1.27), P-trend <0.0001], solid stool FI [HR (95% CI) =1.26 (1.13, 1.41), P-trend <0.0001], and liquid stool FI [HR (95% CI) = 1.19 (1.08, 1.31), P-trend <0.0001] after adjusting for dietary fiber and other covariates (Table 1).

In secondary analyses, the association became stronger when we examined severe (weekly) FI [Q5 vs Q1, Overall FI: HR (95% CI) = 1.25 (1.14, 1.38), P-trend <0.0001, Solid: HR (95% CI) = 1.29 (1.14, 1.45), P-trend <0.0001, Liquid: HR (95% CI) = 1.27 (1.11, 1.45), P-trend = 0.0003] (Table S2). Long term proinflammatory diet represented by the cumulative average EDIP score (1984-2006) was also associated with increased FI risk [Q5 vs Q1, Overall FI: HR (95% CI) =1.10 (1.02, 1.19), P-trend = 0.0006, Solid: HR (95% CI) =1.18 (1.05, 1.32), P-trend =0.0004, Liquid: HR (95% CI) =1.09 (0.99, 1.21), P-trend = 0.007]. We did not observe significant effect modification by the covariates listed in Model 3 (P values for interaction > 0.05).

We observed an increased risk of overall FI, as well as both solid and liquid stool FI, among older women consuming a proinflammatory diet, providing the first prospective evidence identifying proinflammatory dietary pattern as a risk factor for FI.

Fiber supplementation is a first line treatment for FI[10] and dietary fiber may also have a beneficial role in FI prevention.[4] We previously demonstrated that higher fiber intake was associated with lower risk of liquid stool FI but not solid stool FI,[4] perhaps because fiber normalizes stool consistency through water absorption with stool bulking.[10] However, the current study shows that the association of proinflammatory diet with FI was independent of fiber intake and appeared to be stronger for solid (HR: 1.26) than liquid stool FI (HR: 1.19). The pathophysiology of solid and liquid stool FI differ; whereas chronic bowel disturbances are more likely to lead to liquid stool FI, solid stool FI is more influenced by mechanical risk factors such as pelvic floor injury from obstetric trauma.[1, 2] Proinflammatory diet may contribute to liquid stool FI through interactions with gut microbiota and subsequent bowel disturbances.[5, 6] In solid stool FI, proinflammatory diet may have a direct impact on neuromuscular continence mechanisms, as inflammation may diminish the neuromuscular function and integrity of the pelvic floor.[7]

Our study has several strengths, most notably our prospective design with capture of *incident* FI and minimization of reverse influence of *prevalent* FI on lifestyle habits. We also acknowledge some limitations, specifically residual confounding that can occur in any observational study despite controlling for many known and putative FI risk factors.

In summary, dietary modifications aimed at reducing dietary proinflammatory potential may represent an effective FI prevention strategy. Future translational studies are needed to explore the potential role of inflammation in the pathogenesis of FI.

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Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Conflicts of Interest:

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Data availability statement:

The data of this study are available upon reasonable request. Further information including the procedures to obtain and access data from the Nurses' Health Studies is described at https://www.nurseshealthstudy.org/researchers (contact nhsaccess@channing.harvard.edu).

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Table 1.

Pro-inflammatory diet and risk of fecal incontinence in older women (NHS1)

	Quintiles of EDIP score					
	Q1	**Q2**	**Q3**	**Q4**	**Q5**	**P-trend**
Overall						
Person-years	38064	37996	38095	38134	38270	
Cases, n	1215	1327	1379	1461	1514	
Model 1	ref	1.08 (1.00, 1.17)	1.14 (1.06, 1.23)	1.22 (1.13, 1.31)	1.30 (1.20, 1.40)	<0.0001
Model 2	ref	1.06 (0.98, 1.14)	1.09 (1.01, 1.18)	1.14 (1.05, 1.23)	1.17 (1.08, 1.26)	<0.0001
Model 3	ref	1.06 (0.98, 1.15)	1.10 (1.02, 1.19)	1.15 (1.06, 1.24)	1.17 (1.08, 1.27)	<0.0001
Solid stool						
Person-years	38641	38586	38716	38797	38985	
Cases, n	588	683	702	739	738	
Model 1	ref	1.15 (1.03, 1.28)	1.20 (1.07, 1.33)	1.27 (1.14, 1.42)	1.32 (1.19, 1.47)	<0.0001
Model 2	ref	1.13 (1.01, 1.27)	1.17 (1.05, 1.30)	1.23 (1.10, 1.37)	1.24 (1.11, 1.39)	<0.0001
Model 3	ref	1.13 (1.02, 1.27)	1.18 (1.05, 1.31)	1.24 (1.11, 1.38)	1.26 (1.13, 1.41)	<0.0001
Liquid stool						
Person-years	38480	38477	38566	38617	38738	
Cases, n	752	803	860	924	1010	
Model 1	ref	1.06 (0.96, 1.17)	1.15 (1.04, 1.27)	1.24 (1.13, 1.37)	1.38 (1.25, 1.52)	<0.0001
Model 2	ref	1.02 (0.93, 1.13)	1.08 (0.97, 1.19)	1.12 (1.02, 1.24)	1.19 (1.08, 1.31)	<0.0001
Model 3	ref	1.03 (0.93, 1.14)	1.09 (0.99, 1.20)	1.13 (1.03, 1.25)	1.19 (1.08, 1.31)	<0.0001

Notes: Abbreviation: EDIP: Empirical Dietary Inflammatory Pattern; HR: Hazard Ratio; CI: Confidence Interval. Model 1: Cox proportional hazards model stratified by age (continuous, month) and time period (in 2-year intervals); Model 2: Model 1+ race (white, non-white), smoking (never, past, current), body mass index (<18.5, 18.5–24.9, 25–29.9, 30–34.9, 35 kg/m^2), physical activity (<3, 3–8, 9–17, 18—26, 27+ metabolic equivalent of task-hours/week), menopausal hormone use (never users, past users, current users), parity (number of live births), hysterectomy (yes or no), hypertension (yes or no), diabetes mellitus (yes or no), neurologic disease (yes or no), and history of cholecystectomy (yes or no); Model 3: Model 2 + dietary fiber intake. P for trend was calculated using the median of each quintile of EDIP score as a continuous variable. All EDIP scores are energy-adjusted.

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