The Relationship Between Dietary Inflammatory Index and Inflammatory Markers in Patients with Ulcerative Colitis

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Abstract

Objective: This study aimed to evaluate the relationship between dietary inflammatory index scores and inflammatory markers in patients with ulcerative colitis in remission.

Methods: In this cross-sectional study conducted at the Gastroenterology Clinic of Gazi University Medical Center between February and July 2016, we included 44 patients (17 women and 27 men, aged 19–65 years). The average ages were 49.1±11.67 years for men and 45.3±10.7 years for women. The study involved assessing patients' dietary habits and recording their food consumption. Inflammatory markers, including C-reactive protein (CRP) and leukocyte count, were obtained from routine biochemical results. Fecal calprotectin levels were determined by analyzing stool samples collected after face-to-face interviews with patients.

Results: The average CRP levels for men were 4.6±2.56 mg/dL, and for women, 4.4±1.95 mg/dL. The average calprotectin levels were 251.7±240.6 µg/g for men and 322.2±262.66 µg/g for women. We observed positive and statistically significant correlations between the dietary inflammatory index and CRP (r=0.60; P<0.001). Additionally, significant correlations were found between various quartile levels (Q1–Q2, Q1–Q3, Q1–Q4, Q2–Q4, and Q3–Q4) in calprotectin level assessment (rho=0.864, P<0.001).

Conclusion: The dietary inflammatory index significantly influences inflammatory markers and the disease course in patients with ulcerative colitis. However, further comprehensive studies with larger sample sizes are needed to corroborate these findings.

Keywords: Inflammation, dietary inflammatory index, ulcerative colitis

INTRODUCTION

Inflammatory bowel disease (IBD) is an umbrella term for disorders characterized by chronic inflammation of the digestive tract.¹ Ulcerative colitis (UC) specifically refers to inflammation and ulceration along the superficial lining of the colon and rectum. In contrast, Crohn’s disease typically involves inflammation of the digestive tract lining, often affecting deeper layers.² While the exact causes of these diseases remain unidentified, a combination of genetic and environmental factors is believed to play a crucial role in their development. Notable environmental triggers include the transition to modern lifestyles, the use of oral contraceptives, smoking habits, and dietary patterns.¹

Nutritional habits play a significant role in the development and prognosis of IBD.³ Diets rich in fats, fried foods, refined carbohydrates, and animal products are known to increase the risk of IBD.⁴ Conversely, high-fiber diets and sufficient consumption of fruits and vegetables are associated with a reduced risk.⁵ Certain dietary factors can trigger immunological responses that contribute to the development of IBD. These include the consumption of cow’s milk, refined sugar, reduced vegetable intake, and high-fat diets.⁶

The impact of dietary habits on disease prognosis is mediated through pro-inflammatory and anti-inflammatory mechanisms. Western dietary patterns, characterized by the consumption of simple sugars, fried foods, high-fat foods, and refined grains, are known to elevate inflammation markers. In contrast, the Mediterranean diet, which includes whole grains, dark green leafy vegetables, low meat consumption, moderate alcohol intake, and olive oil, has been reported to decrease inflammation markers.⁷

The Dietary Inflammatory Index (DII) is a tool established based on the effects of consumed food on inflammation markers, as validated in a specific study.⁸ Research exploring the relationship between DII and inflammatory markers has been conducted in individuals with various health conditions, including cardiovascular diseases, cancer, asthma, metabolic syndrome, and bowel diseases.⁹⁻¹¹ In the context of UC, C-reactive protein (CRP) and fecal calprotectin levels are critical inflammatory markers used in patient monitoring. Calprotectin, a calcium-binding protein found in neutrophils, offers a cost-effective, sensitive, and simple method for detecting and monitoring intestinal inflammation.¹² This study aims to...
evaluate the relationship between DII scores and inflammatory markers in patients with UC who are in remission.

METHODS
Study Group
This cross-sectional study was conducted at the Gastroenterology Clinic of Gazi University Hospital, focusing on patients with ulcerative colitis in remission. The study took place between February and July 2016.

The participant group comprised 17 females and 27 males, ranging in age from 19 to 65 years. The exclusion criteria included having another inflammatory disease, any chronic disease, being a pregnant or breastfeeding woman, and being elderly (over 65 years). The determination of whether patients were in remission was made by a gastroenterologist, based on colonoscopy or rectoscopy results and the absence of complications in the patient. Only those patients who were confirmed to be in remission were included in the study.

The study’s protocol was developed in adherence to the Declaration of Helsinki and received approval from the Ethical Committee for Clinical Investigations of the Zekai Tahir Burak Women’s Health Training and Research Hospital, under the T.C. Ministry of Health. This approval was granted by the Scientific Ethics Committee, as per Decision 62/2015, dated 22 December 2015.

Nutritional Status
In this study, volunteers were asked to complete a questionnaire that included questions on socio-demographic variables, health status, disease history, frequency of food consumption, cooking methods, and types of oils used. This was followed by a face-to-face interview with the researcher. Starting the day after the interview, the participants recorded their food consumption for a duration of 7 days. Detailed instructions were provided to the participants on how to accurately record their food intake, and the investigator made daily phone calls to confirm each record. The food consumption data was based on the participants’ reports.

For the evaluation of food consumption, the study utilized the Nutrition Information System (BEBIS). However, since the standard BEBIS database lacks information on the quantities of certain nutrients with inflammatory properties, a new database was created using data from the United States Department of Agriculture (USDA), specifically focusing on the evaluation of flavonoid content.

Anthropometric Measurements
Anthropometric measurements, including body weight (in kilograms, kg) and height (in centimeters, cm), were taken for each participant in the study. These measurements were conducted by the researcher, adhering to standardized techniques. Body mass index (BMI) was calculated for each individual; it is a value derived from a person’s weight and height. BMI is defined as the body mass (weight) divided by the square of the body height. This index is expressed in units of kg/m², with weight in kilograms and height in meters (m).

Biochemical Findings
For the study participants, CRP levels and leukocyte counts were obtained from routine blood test results. To assess the calprotectin levels, stool samples were collected from the participants on the day of the study. These samples were then stored at -80°C in the Biochemistry Laboratory at Gazi University Hospital. Once stool samples from all participants had been collected, the analysis was conducted simultaneously. The assessment of calprotectin levels was performed using the Ridascreen calprotectin kit, employing the Enzyme-Linked Immunosorbent Assay (ELISA) method.

Dietary Inflammatory Index
DII scores in this study were calculated using the nutrient inflammatory index scores established by Cavicchi et al.15 To determine the DII score, the amount of nutrients recorded from the participants’ food consumption was multiplied by the reference values provided in Cavicchi et al.’s methodology. The resulting score was then divided by 100, as outlined in the reference method.

In our analysis, the DII score encompassed a range of dietary components: dietary energy, garlic, ginger, turmeric, tea, caffeine, wine, beer, other forms of alcohol, carbohydrates, fiber (pulp), fats, omega-3 fatty acids, omega-6 fatty acids, monounsaturated fatty acids, saturated fatty acids, proteins, cholesterol, vitamins A, B₁₂ (thiamine), B₂ (riboflavin), B₃ (niacin), B₆, B₇ (folic acid), B₉, C, D, E, beta carotene, and minerals such as magnesium, zinc, iron, and selenium. It also included flavonoids and phytoestrogens like quercetin, lutein, genistein, daidzein, cyanidin, and epicatechin. The reverse value of the final score was interpreted as indicative of the inflammation index score of the participants’ diets.

Statistical Analysis
Statistical analysis was performed with the program SPSS 22.0 16. For descriptive statistics, statistics, frequencies and percentages were used for qualitative observations, and comparisons were made with chi-square tests. For quantitative observations, the Mann–Whitney U test was used in double groups considering the number of observations. The ANOVA test was used to compare two or more independent groups with normal distributions; the mean is shown with the standard deviation. In the evaluation of diet inflammation index, quartiles were used. Dietary inflammatory index scores are in ascending order: (Quartile) Q₁ (< -2.93), those in the 25–50% percentile group as Q₂ (-2.93 to -2.27), those in the 50–75% group as Q₃ (-2.27 to -1.86) and those in the 75–100% as Q₄ (> -1,86) group were also qualified.

RESULTS
The average age of the participants was 47.6±11.3 years. A majority of the patients were male, constituting 61.4% of the study group. In the lower dietary inflammatory index quartiles (Q₁ and Q₂), there was a higher proportion of women compared to men. Conversely, in the higher quartiles (Q₃ and Q₄), the proportion of men surpassed that of women. Over half of the individuals (63.6%) had been living with their condition for 15 years or more. Detailed characteristics of the participants are presented in Table 1.

Regarding serum inflammation markers, the average CRP levels were 4.6±2.56 mg/dL in men and 4.4±1.95 mg/dL in women (P<0.005). The calprotectin levels averaged 251.7±240.6 mg/dL for men and 322.2±262.66 mg/dL for women (P<0.005), as shown in Table 2.

When evaluating the CRP levels of individuals across dietary inflammatory index (DII) quartiles, notable differences were observed. The mean CRP level in Quartile 1 (Q₁) was 3.0±0.8, while in Quartile 4 (Q₄), it was significantly higher at 6.1±2.7 (P<0.05). In Quartile 2 (Q₂), the mean CRP level was 4.0±1.8, and in Quartile 3 (Q₃), it was 4.9±2.4. Statistical analysis revealed no significant differences between the quartiles, with the exception of Q₁ and Q₄ (P=0.05), as detailed in Table 3.
The mean calprotectin levels for Q1 through Q4 were 64.6±36.2, 218.7±199.4, 237.8±186.2, and 578.7±190.4, respectively. Statistically significant differences were observed between these pairs: Q1–Q2, Q1–Q3, Q1–Q4, Q2–Q4, and Q3–Q4 (P<0.05).

Furthermore, a moderate positive correlation was found between the dietary inflammation index and CRP levels (r=0.60; P<0.001). For DII values ranging from -6 to -5, CRP levels were between 2 and 4. For DII values from -4 to -3, CRP levels were between 3 and 4. When DII values ranged from -3 to -2, CRP levels were between 3 and 6. For DII values between -2 and 1, CRP levels exceeded 8, as illustrated in Figure 1.

**DISCUSSION**

DII is a tool used to assess the impact of consumed foods on inflammatory markers, with DII levels fluctuating in tandem with these markers. While DII has been calculated in various diseases characterized by chronic inflammation, such as asthma, cardiovascular diseases, cancer, and diabetes, its application in ulcerative colitis has not been extensively explored.

Nutritional factors can influence bodily inflammatory markers through both pro-inflammatory and anti-inflammatory mechanisms. Typical Western diets, rich in simple sugars, fried foods, high-fat items, and...
refined grains, are known to elevate inflammatory markers. On the other hand, Mediterranean diets, which include fruits, vegetables, whole grains, legumes, nuts, and olive oil, have been shown to reduce dietary inflammatory markers.7

The primary goal in the treatment of ulcerative colitis is to maintain patient remission.19 Since the DII directly influences inflammatory markers within the body, adhering to a diet with a low dietary inflammation index is crucial for keeping individuals in remission.20 This highlights the significance of dietary choices in managing and potentially alleviating the symptoms of ulcerative colitis.

Numerous studies have utilized DII developed by Cavicchia et al.14; however, the calculation of scores varies across research. In the work of Cavicchia et al.13, DII scores ranged from -20.9 to 24.7. Shivappa et al.8 however, the calculation of scores varies across research. In the work of Cavicchia et al.13, DII scores ranged from -20.9 to 24.7. Shivappa et al.8 reported a range of -5.4 to 5.8, Wirth et al.21 had a range from -62.7 to 5.89, and Ruiz-Canela et al.22 found a range of -4.9 to 3.7. In our study, scores ranged from -5.13 to -0.17. Consistent with other research, our study indicates that dietary factors have anti-inflammatory effects when considering the scores of all participants. Factors contributing to these anti-inflammatory properties include the consumption of certain fats, notably omega-9 fatty acids and saturated fats, as well as specific food cooking methods such as oven baking, grilling, and boiling. The study also identified the intake of anti-inflammatory foods—namely proteins, omega-3 and omega-9 fats, energy sources, simple carbohydrates, and saturated fats—as protective against the pro-inflammatory effects of certain nutrients. These pro-inflammatory nutrients include vitamin A, vitamin E, riboflavin, vitamin B3, vitamin C, beta-carotene, flavonoids, niacin, thiamine, magnesium, zinc, selenium, various fatty acids, omega-6 fatty acids, cholestero, and vitamin B12.

Serum CRP is an increased inflammatory marker in ulcerative colitis patients. CRP levels are significantly elevated in exacerbated patients.23 In Chang et al.24, average CRP in ulcerative colitis patients was 0.53±0.882 mg/dL. In Masoodi et al.25, it was 2.75±6.09 mg/dL. In our study, it was 4.6±2.56 mg/dL for men and 4.4±1.95 mg/dL for women, higher than in other studies. The reference range for CRP in the laboratory was 0–6 mg/dL. This is due to the presence of serum CRP levels during the patients’ remission period.

Calprotectin, a calcium-binding protein found in neutrophils, has been shown to increase in concentration in patients with ulcerative colitis. The fecal calprotectin test offers a cost-effective, sensitive, and straightforward method for detecting and monitoring intestinal inflammation. A calprotectin level above 50 μg/g is considered elevated and indicative of significant inflammation.26 In the research conducted by Chang et al.24, the average calprotectin level was reported to be 497.4±584.8 μg/g, while Schepfer et al.27 documented an average of 246 μg/g. In line with these findings, our study revealed mean calprotectin levels of 251.7±240.6 μg/g in men and 322.2±262.66 μg/g in women.

During intestinal inflammation in ulcerative colitis, leukocytes permeate the mucosa, resulting in the excretion of neutrophil-derived proteins in the stool.28 Fecal calprotectin levels up to 155 μg/g are deemed normal for UC patients in remission. However, levels may rise during periods of acute inflammation and serve as a significant indicator of disease activity; calprotectin is markedly elevated during active disease stages.29 In our study, calprotectin levels were marginally above 155 μg/g, suggesting the possibility of acute inflammatory episodes.

Studies have explored the relationship between various diseases—including cancer, metabolic syndrome, asthma, cardiovascular disease, and bowel diseases—and the Dietary Inflammatory Index (DII).7,8,11,12 Shivappa et al.8 investigated the association between CRP levels and the DII. They categorized DII scores into three groups and found a statistically significant increase in the DII with higher levels of CRP. In a similar vein, Shivappa et al.30 reported that a higher DII corresponded to an increase in the pro-inflammatory nature of diets, which was significantly related to increased CRP levels in the pro-inflammatory group as compared to the group with anti-inflammatory dietary properties.30 A study in Turkey involving hemodialysis patients also examined the relationship between CRP and DII and divided the subjects into three DII groups, finding a statistically significant positive correlation between DII and CRP.31 Graaf et al.32 noted that while diet quality correlated with fecal calprotectin levels in IBD and various gastrointestinal (GI) symptoms in irritable bowel syndrome (IBS), the inflammatory potential of the diet was only associated with GI symptoms in IBD. Conversely, Mirmiran et al. found no significant relationship between DII and disease activity in patients with IBD.

Elevated levels of CRP can indicate the onset of an inflammatory episode. CRP levels rise as an acute phase response to various pathophysiological conditions, including infection, cell damage, and neoplasms22,33, as well as to the Dietary Inflammatory Index (DII).8 Since achieving and maintaining remission is the primary goal of ulcerative colitis treatment, monitoring the DII is a crucial aspect of nutritional therapy. Our study reveals a statistically significant correlation between the DII and CRP levels, which is most apparent when contrasting Quartile 1 (Q1) with Quartile 4 (Q4). Quartiles 2 (Q2) and 3 (Q3) display similar patterns. The anti-inflammatory features between Q1 and Q4 are markedly distinct, with one contributing factor being the excessive consumption of foods high in cholesterol, energy, and saturated fat.

Previous studies with IBD patients4,11 have employed food frequency questionnaires to calculate the DII. In our research, we utilized a 7-day food consumption record, which provides more precise results for calculating the DII. Contrary to other studies, we believe the pivotal factor in the relationship observed between the DII and biochemical markers in our study is attributable to the method of food consumption recording.

CONCLUSION
The results of this study are novel since this is the first study to evaluate DII relationships in ulcerative colitis patients. In this study, inflammatory markers were used to track dietary inflammation indices. In order to decrease CRP and calprotectin, DII can be used to improve follow-up treatment. The planned diet should be as anti-inflammatory as possible. In the future, similar nutritional therapy could be done for the Mediterranean diet, in addition to Western diets. Adequate and balanced nutrition, macro and micronutrients, and adequate pulp intake are important. Preparing and cooking methods are also important: frying and roasting are preferred over boiling, baking, and grilling.

Calprotectin levels are significantly elevated during an active episode in individuals with inflammatory conditions, yet there is a lack of published research on the connection between calprotectin levels and diet. In this study, we found a positive and statistically significant correlation between DII and calprotectin levels, with both factors showing parallel trends. The DII may thus serve as a valuable guide in tailoring individual treatments and reducing inflammatory markers.
This pilot study is crucial as it lays the groundwork for future research. For subsequent studies, it would be advantageous to increase the sample size, ensure a normally distributed cohort in terms of socioeconomic characteristics, and incorporate a control group. Moreover, it’s important to thoroughly assess the dietary habits of participants, implement specific nutritional plans, and monitor the impact on inflammatory markers.

**Ethics Committee Approval:** The study’s protocol received approval from the Ethical Committee for Clinical Investigations of the Zekai Tahir Burak Women’s Health Training and Research Hospital (Approval Number: 62/2015, Date: 22.12.2015).

**Informed Consent:** Written informed consent was obtained from the patients participating in this study.

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