Dietary Intervention in Management and Remission of Ulcerative Colitis: A Systematic Review

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Abstract

Ulcerative Colitis (UC), an Inflammatory Bowel Disease (IBD) affecting the colon, is characterized by recurring inflammation in the colon's inner lining. Common symptoms include blood in the stool and diarrhea. Immune responses, gut microbes, and environmental factors contribute to UC's development. Disease relapses impact patients' quality of life. Studies link diet factors like soft drinks, fatty acids, and low fruit/vegetable intake to UC. Promising diets like Specific Carbohydrate Diet (SCD), Low Fermentable Oligosaccharide, Disaccharide, Monosaccharide, and Polyol (FODMAP), and Inflammatory Bowel Disease-Anti-Inflammatory Diet (IBD-AID) positively affect symptom management. Following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) 2020 guidelines, the review searched PubMed and PubMed Central. The screening process identified pertinent articles that were subsequently evaluated for quality before incorporation. Our study has demonstrated that following an anti-inflammatory diet holds the potential to avert subclinical colonic inflammation in UC patients who are in clinical remission. This finding is supported by notable changes in the metabolic and gut microbial compositions among individuals who adhere to the anti-inflammatory diet. The research comprehensively explores the impact of diet on UC, aiming to establish its connection with UC occurrence. It seeks to identify a specific dietary plan for UC individuals and assess its effects on their health. The study also investigates the anti-inflammatory diet's role in UC remission. Evidence shows the anti-inflammatory diet prevents colonic inflammation in UC patients in clinical remission. This finding, accompanied by metabolic and microbial changes, encourages future well-structured trials to assess dietary intervention efficiency in UC remission.

Introduction & Background

Ulcerative colitis, a form of inflammatory bowel disease, is a long-lasting inflammatory condition affecting the colon, with its cause remaining unknown (idiopathic). The main feature of UC is the recurring pattern of inflammation in the colon's inner lining [1]. The prevalence of UC is on the rise in Western nations by 0.5%, and there is a swift uptick in the occurrence of IBD in newly industrialized Asian countries like Japan, South Korea, and China, as well as in Central and South America. The growing number of individuals worldwide affected by UC is a significant cause for concern. The primary symptoms observed in UC patients are the presence of blood in the stool and episodes of diarrhea. The development of UC involves multiple factors, including genetic predisposition, defects in the protective epithelial barrier, disrupted immune responses, imbalances in gut microbes, and environmental influences [2,3].

The influence of environmental factors in the development of IBD has been proposed. Factors like mode of birth, breastfeeding, exposure to antibiotics, air pollution, smoking, psychological state, exercise, and diet during early life and beyond are believed to be potential contributors to IBD pathogenesis or disease activity [4].

Multiple disease relapses in patients with IBD have been shown to impact their quality of life negatively [5] and increase the risk of colitis-associated colorectal cancer, particularly in those with longstanding UC and Crohn's colitis [6]. The initial extensive meta-analysis evaluating the risk of colorectal cancer (CRC) in individuals with inflammatory bowel disease (IBD) found a 2% risk at 10 years following the diagnosis of ulcerative colitis, an 8% risk at 20 years, and an 18% risk at 30 years from the onset of colitis. Nevertheless, contrasting research indicates that the incidence of CRC in ulcerative colitis patients may be decreasing. Many UC patients believe that their diet influences their disease relapses, and several studies, primarily observational and retrospective, have identified specific dietary factors associated with an elevated risk of UC relapse [7].

Recent meta-analyses have unveiled significant insights into dietary factors and their links to ulcerative colitis (UC) development. Soft drink consumption and sucrose intake were associated with a 69% and 10% increased UC risk, respectively. Conversely, the consumption of fruits and vegetables was associated with a reduced UC risk. Another meta-analysis involving seven epidemiological studies found a substantial relationship

between meat consumption, particularly red meat, and a higher UC risk. Additionally, diets rich in n-3 polyunsaturated fatty acids (PUFAs) were linked to a lower UC risk, while dietary arachidonic acid, an n-6 PUFA measured in adipose tissue, was associated with an elevated UC risk in a Danish adult cohort study [8].

Several diets have been outlined that have demonstrated promising outcomes within the IBD community. These include the SCD, the low FODMAP diet, the Paleolithic diet (Paleo), and the anti-inflammatory diet (IBD-AID) [9]. A comprehensive review of approximately 30 studies was conducted to assess the effectiveness of the mentioned supplements and their impact on gastrointestinal disease. The analysis revealed that the incorporation of dietary fibers, polyphenols, and fatty acids, along with adhering to a low-sugar diet, can enhance the quality of life and trigger clinical remission in individuals suffering from ulcerative colitis. Despite their positive effects on IBD symptom alleviation and management, it is essential to examine substances for their potential benefits and drawbacks in the context of IBD. Such substances encompass probiotics, polyphenols, dietary fibers, fatty acids, and specific low FODMAP diets, which will be explored in the following discussions.

Despite these observations, a recent Cochrane systematic review highlights the need for a consensus on evidence-based dietary interventions for UC patients. More high-quality, well-powered, randomized, controlled trials are required to thoroughly assess dietary interventions' efficacy [10].

Certainly, we are exploring various diet types and their impact on the management of (UC).

Research Question

Comparing the efficacy of diet in the management and remission of UC:

The relationship between diet and ulcerative colitis (UC) has been a subject of growing interest in recent research. Our study explores how dietary choices may influence the course of UC and its symptoms. These investigations typically involve examining specific diets tailored to UC cases, with an emphasis on factors like fiber intake, polyphenols, fatty acids, and FODMAP. Researchers aim to determine whether adhering to these diets can contribute to improved overall health and symptom management in individuals with UC.

Clinical Implications

The outcomes provide valuable insights into the potential impact of diet as a complementary strategy in the management and remission of UC, shedding light on whether specific dietary interventions can enhance the well-being of UC patients or potentially exacerbate their condition.

Methods

Our method and results for systematic review are reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA)2020 guidelines [19].

Search Strategy

We searched PubMed/Medline, PubMed Central (PMC), and ScienceDirect to identify full-text relevant published papers. They were meticulously searched using appropriate keywords and medical subject headings (MESH) terms to find all potentially relevant articles demonstrating the dietary intervention in the management of UC. The MESH strategy used in PubMed was: "Colitis, Ulcerative"/classification"[Majr] OR "Colitis, Ulcerative/complications"[Majr] OR "Colitis, Ulcerative/diet therapy"[Majr] OR "Colitis, Ulcerative/genetics"[Majr] OR "Colitis, Ulcerative/history"[Majr] OR "Colitis, Ulcerative/immunology"[Majr] OR "Colitis, Ulcerative/metabolism"[Majr] OR "Colitis, Ulcerative/microbiology"[Majr] OR "Colitis, Ulcerative/mortality"[Majr] OR "Colitis, Ulcerative/pathology"[Majr] OR "Colitis, Ulcerative/physiopathology"[Majr] OR "Colitis, Ulcerative/prevention and control"[Majr] OR "Colitis, Ulcerative/therapy"[Majr])) AND ("Diet/adverse effects"[Majr] OR "Diet/classification"[Majr] OR "Diet/history"[Majr] OR "Diet/methods"[Majr] OR "Diet/mortality"[Majr] OR "Diet/statistics and numerical data"[Majr]).

-After retrieving all papers and rigorously checking references to ensure that no potentially relevant publications were overlooked, the titles, abstract, and subjects' headings were reviewed for relevance, primary and secondary outcomes were identified, and the data was extracted by the corresponding authors. Any differences in data extraction were settled through consensus.

Inclusion and Exclusion Criteria

The selection choice is from randomized control trials (RCTs) published from 2018 to 2023. All selected articles were peer-reviewed and published in the English language. Grey literature was excluded. Our selection for eligibility followed the population, intervention, comparison, and outcomes (PICO)model.

The inclusion and exclusion criteria are shown in **Table 1**.

Inclusion Criteria	Exclusion Criteria
1-Adult age patients between (15-80) with Ulcerative colitis	**1**-Childeren (age less than 15).
2- The research is published in the last 5 years	**2**-patients who receiving any kind of chemotherapy
3-Patient is taking treatment for UC	**3**- Patients who have an organ transplant
4-Patients from any geographic region	**4**-patients who have any other auto-immune diseases
5-Patients are taking a variable kind of food	**5**-Studies that were conducted before 2017
6-Systematic review and observational studies were included	**6**-Articles on guidelines

Table 1 shows the inclusion and exclusion criteria used for selecting the articles.

Data Extraction

The retrieval and review were completed by two separate researchers independently. In the case of disagreements, the researchers would discuss the data for its relevance and design to eligibility criteria to reach an accord. A third researcher was counseled for objectivity if a decision could not be made.

Quality Assessment

This systematic review included RCT, case-control, case series, case report, and cohort studies. During the selection of papers, appropriate quality appraisal tools were utilized to check for bias. Only those articles were chosen that satisfied > 70% of the criteria.

Critical Appraisal of Studies

We critically appraised our screened articles using:

1. Quality assessment of case-control, case series, and case report by using the Joanna Briggs Institute (JBI) assessment tool [11] in Table 2.

Author	Type of Study	Quality appraisal tool	1	2	3	4	5	6	7	8	Quality %
Chiba et al. [12]	Case series	Joanna Briggs Institute (JBI)	Yes	yes	yes	yes	No	No	yes	yes	75%
Glabska et al. [13]	Case-control	Joanna Briggs Institute (JBI)	Yes	yes	yes	yes	yes	yes	yes	yes	100%
Jian et al. [14]	Case-control	Joanna Briggs Institute (JBI)	yes	yes	yes	yes	No	No	Yes	Yes	75%
Morton et al. [15]	Case report	Joanna Briggs Institute (JBI)	yes	yes	yes	yes	yes	No	No	yes	75%

Yes= low risk, No= High risk

Table 2 shows the quality check using the JBI assessment tool.

2. The Cochrane risk of bias tool [16]. The bias risk assessment looked at seven causes of potential bias, and a summary was given for each randomized clinical trial (RCT) in this review in Table 3.

Article	Random sequence generation – Selection Bias	Allocation of concealment – Selection bias	Blinding of both participants and evaluators – Performance Bias	Blinding of assessment during outcome collection – Detection bias	Incomplete outcome data – Attrition Bias	Selective reporting – Reporting Bias	Quality %
Keshtel et al. [5]	Low risk	Low risk	Low risk	Low risk	High risk	Low risk	80%
Naftali et al. [17]	Low risk	Low risk	Low risk	High risk	Low risk	Low risk	80%

Table 3 shows the quality check using the Cochrane Risk of Bias tool.

3. Quality assessment of Systematic review by using the Scale of the Assessment of Narrative Review Articles (SANRA) checklist assessment tool [18] in Table 4.

Author	Type of Study	Quality appraisal tool	1	2	3	4	5	6	Quality
Keshtel et al. [1]	Systematic review	SANRA	2	1	2	2	1	2	Minimal risk (10)
Malinowski et al. [9]	Systematic review	SANRA	2	2	2	2	1	2	Minimal risk (11)

Using categories 0-2 on the scale to imply low or high quality. Maximum Sum score is twelve for the highest quality.

Table 4 shows the quality check using the SANRA checklist assessment tool.

Results

Literature Search and Study Selection

The MESH strategy generated 3021 articles from keywords, eligibility criteria, and databases. This systematic review was conducted following the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines [19]. Eight articles were excluded due to duplication. After filtering to include articles from the last five years only, as the guidelines vary consistently, we were left with 613 articles. Upon reading the titles and abstracts, 523 articles were excluded. Of the remaining articles, 26 were excluded because they were unrelated to UC. Thirty-nine articles were excluded because of only medication induction, and 1 was excluded because of age group. Eight final articles met the criteria and were included. Our PRISMA flow diagram is shown below in Figure 1.
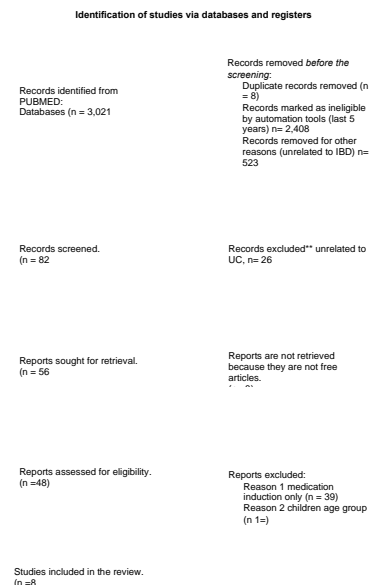
Identification of studies via databases and registers

Records identified from PUBMED:
Databases (n = 3,021)

Records removed *before the screening:*
Duplicate records removed (n = 8)
Records marked as ineligible by automation tools (last 5 years) n= 2,408
Records removed for other reasons (unrelated to IBD) n= 523

Records screened. (n = 82)

Records excluded** unrelated to UC, n= 26

Reports sought for retrieval. (n = 56

Reports are not retrieved because they are not free articles.

Reports assessed for eligibility. (n =48)

Reports excluded:
Reason 1 medication induction only (n = 39)
Reason 2 children age group (n 1=)

Studies included in the review. (n =8

Fig. 1 shows the PRISMA flow diagram.

*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).

**If automation tools are used, indicate how many records were excluded by a human and how many were excluded by automation tools.

Relapse: a flare-up needing stronger treatment. The reappearance of blood isn't a relapse if it resolves with previous measures like medication, diet, or lifestyle changes.

Remission: Symptomatic improvement until resolution.

-A brief overview of the studies included is given in **Table 5**

Showing baseline characteristics of the studies included.

Table 5 shows an overview of the characteristics of the selected articles.

Discussion

Dietary Interventions in UC

Despite the contribution of various –omics fields like genomics, metagenomics, transcriptomics, proteomics, and metabolomics to the IBD pathogenesis research, the mechanisms through which diet influences inflammation and remission in UC patients remain unexposed [33]. In their 2019 study, Keshtel et al. [1], shed light on the pivotal role of diet in the management of the symptoms and the condition in IBD patients [32]. A comprehensive review of the RCTs that have investigated the effectiveness of diet in inducing or maintaining remission or improving the symptoms in patients with UC suggests that diet as an environmental factor plays a crucial role in the pathophysiology of IBD (particularly UC). Problematic foods like spices, onion, cabbage, alcohol, fried/fatty foods, and caffeine trigger gut symptoms in both IBD and IBS.

The Western diet, high in unhealthy saturated fats and low in fruits and vegetables, is thought to increase the risk of IBD, such as UC, due to its pro-inflammatory effects [20]. In the RCT by Keshtel et al. [5], a six-month study, it was found that AID helped maintain or even slightly reduce the levels of the inflammatory marker fecal calprotectin (FCP) which is a predictor of relapse in UC patients. However, a previous study found no significant differences in clinical relapse rates with AID [21]. The AID was designed based on the exclusion of specific dietary products associated with UC risk like red/processed meat, antioxidants, fiber, and n-3 PUFA [22]. A better understanding of the mechanisms through which these products contribute to flare-ups in UC patients helps us design specific dietary protocols for preventing relapse and maintaining remission.

On the other hand, studies by Malinowski et al. [9], and Morton et al. [15], showed that a low FODMAP diet is associated with reduced inflammation and good symptom control in UC patients. This could be attributed

to low fermentable carbohydrate levels in the diet. It includes meat, dairy, gluten-free grains, fruits, veggies, nuts, and spices. Although there is strong evidence in support of a low FODMAP diet, the long-term impact is unsettled [30].

In the study by Chiba et al. [12], they assessed 8 items for IBD prevention (vegetables, fruits, pulses, and others) as positive contributors (PBDS+), and 8 items (meat, processed meat, and others) as negative contributors (PBDS-). Scores of 5, 3, and 1 were given based on the consumption frequency. The PBDS summed these scores, ranging from -40 to +40, with higher score indicating greater adherence to PBD. They recognized that patients with PBD had relapse rates of 14% and 27% at one and five years respectively. These rates of relapse were much lower even after six years compared to the prevailing therapies in Europe. Therefore, it can be concluded that adherence to PBD in conjunction with the standard medication is an effective therapeutic strategy for preventing UC relapses.

Two RCTs found that a dairy-free diet has not been very successful in reasonably reducing the relapse rate [34,35]. Moreover, most of the exclusion-based diets pose a risk of nutritional deficiency as they add to the existing problem of malabsorption of these nutrients. Calcium deficiency with dairy-free diet is one of the examples of these exclusion-based diet-associated nutritional deficiencies. Healthcare professionals need to be aware of these challenges and educate patients on the potential risks of elimination-based diets.

An exception to this could be the IgG-based exclusion diet. In a case control by Jian et al. [14], an IgG-based exclusion diet showed potential for improving UC symptoms, although IgG antibody levels did not significantly decrease in 6 months. Notable clinical improvements were observed in stool frequency, rectal bleeding episodes, mucosal appearance, and physician assessment using Mayo score. Endoscopic improvement, while not statistically significant, was also noted. After the intervention, the study group had higher BMI and albumin levels, likely due to reduced gastrointestinal discomfort and enhanced absorptive function. This emphasizes the need for proper dietary interventions in UC patients for optimal, long-term management of UC patients.

Impact of Supplements in UC Remission

Cannabinoids can enhance colitis by producing an anti-inflammatory impact. This is accomplished by activating cannabinoid receptors CB1 and CB2, inhibiting enzymes that degrade endocannabinoids (Monoacylglycerol lipase and fatty acid amid hydrolase), and stimulating other receptors like G protein-coupled receptor 55 (GPR55) and Transient receptor potential vanilloid 1 (TRPV1).

In a study by Naftali et al. [17], THC-rich cannabis was used, indicating a primarily central rather than peripheral effect. This could explain the relatively weaker anti-inflammatory outcome observed. Alternatively, the quick onset of central clinical effects might contrast with the longer timeframe needed for anti-inflammatory responses. Consequently, the study's relatively short duration (8 weeks) may not capture peripheral inflammatory changes. In Malinowski et al.'s study [9], curcumin from Curcuma longa showed anti-inflammatory potential for UC patients. Hanai et al. [25], found that 1-gram doses of curcumin alongside mesalamine lowered relapse rates [25]. Resveratrol, found in grapes, blueberries, and peanuts, reduced oxidative stress and improved UC disease activity in research by Samsamikor et al. [26].

Higher levels of docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) replace pro-inflammatory compounds, aiding inflammation resolution. Scaioli et al.'s [29] trial showed that EPA-FFA led to clinical remission and reduced calprotectin levels. Polyphenols found in fruits, vegetables, cereal, coffee, and red wine act as potent antioxidants, surpassing vitamins C and E in protective capacity [24]. Various fibers like fructans, psyllium, and oat bran have been studied for UC. Fructans improved disease activity, psyllium alleviated symptoms, and oat bran enhanced intestinal barrier [27,28].

The Impact of Diet on Gut Microbiota and Mucosal Immune System

Probiotics, live bacteria ingested for health, restore gut balance disrupted in conditions like UC. Probiotic use leads to a decrease in certain bacteria like Bifidobacterium and an increase in others like Escherichia coli, aiding the balance. In Malinowski et al.'s study [9], probiotics showed potential in reducing the need for UC-related steroid use, hospitalizations, and surgical interventions. Promising options in this regard include VSL#3 and Lactobacillus reuteri [23]. The study highlights the connection between probiotics and mucosal immune systems thereby helping us fully understand their role in IBD. A carrageenan-free diet was associated with reduced UC relapse rates in patients in remission. Carrageenan, a seaweed-derived polysaccharide used in the food industry, has potential negative effects including hindering protein absorption, disrupting epithelial function, and promoting intestinal inflammation.

Impact of Patient Knowledge and Attitude Towards Diet

The study by Morton et al. [15], notes that people with IBD often avoid fruits and vegetables due to concerns about fiber and digestive symptoms. Certain highly fibrous foods were linked to initiating or worsening IBD symptoms by the participants. The study also highlights how cooking methods correlate to IBD symptoms. Fried food, alcohol, fruit juice, chili sauce, and caffeine often trigger discomfort. Unique reactions to coffee and tea suggest the need for detailed investigations into their effects on IBD symptoms.

However, in Glabska et al.'s study [13], which compared male UC patients in remission to healthy controls, minor differences in food intake were found. These differences didn't significantly affect nutrient intake. UC patients tended to avoid certain foods, but their diets lacked consistency and balance, raising concerns about nutritional deficiencies. Adequate nutrient intake is crucial for IBD patients to prevent deficiencies and maintain health. Notably, UC patients consumed more potatoes and sugar and commonly excluded dairy, which could impact calcium intake and raise osteoporosis risk.

Importance of Dietary Patterns and Adherence

According to Morton et al. [15], UC patients steer clear of whole grains, spices, alcohol, caffeine, gluten, and dairy products. This helps by lowering the antigenic load and facilitating digestion, aligning with the principles of enteral nutrition (EN) [31].

AID and PBD are associated with reduced rates of relapse in UC patients. Low FODMAP diet and IgG-based exclusion diet are associated with better symptom management and clinical profile in UC patients. The long-term effects of low FODMAP diet in UC patients remain unclear and longitudinal studies with larger sample sizes are needed to assess these effects. It is important to note the possible deficiencies with exclusion-based diets. Another encumbrance to dietary interventional management of UC is the inhabitance of inherent food taboos in individual patients. All these factors need to be considered when planning on a dietary plan in an IBD/UC patient. Taking the geographical bearings, available local produce, and economic status of the patient into account when advocating a particular diet is also a vital factor in determining the adherence to the prescribed diet in these patients. Despite these challenges, dietary intervention remains one of the most economical means of managing IBD/UC.

The systematic review has certain limitations. To maintain research currency, all studies conducted before 2017 were deliberately excluded. Specific groups were excluded based on the study's criteria. For instance, individuals below the age of 15 were not included as participants. Patients undergoing chemotherapy or having undergone organ transplantation were also excluded, along with those diagnosed with other autoimmune diseases. Additionally, articles solely focused on guidelines were not considered. Studies not in English and those absent from the database search, along with unpublished, non-peer-reviewed, and grey literature articles were likewise omitted.

Conclusion

The study delves into a comprehensive analysis of various aspects of diet and its impact on individuals with Ulcerative Colitis (UC). The primary focus is on establishing a clear relationship between diet choices and the occurrence of UC. Additionally, the research aims to determine the specific dietary regimen that will be implemented throughout the study for individuals affected by UC. A crucial facet of the investigation involves assessing whether adopting a particular diet leads to an enhancement or deterioration in the overall health of UC patients. Furthermore, the study examines the role of the anti-inflammatory diet in facilitating remission and the ongoing management of UC. By addressing these research questions, a deeper understanding of the intricate connections between diet, disease management, and patient well-being within the context of UC is anticipated. We have evidence that adherence to an anti-inflammatory diet has the potential to prevent subclinical colonic inflammation in UC patients who have achieved clinical remission. This discovery is complemented by significant alterations in the metabolomic and gut microbial profiles of individuals following the anti-inflammatory diet. These findings hold promise and should catalyze the future development of robustly designed randomized controlled trials (RCTs) involving larger cohorts. These trials will offer a more thorough evaluation of the effectiveness of dietary interventions in maintaining remission among UC patients.

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