

## The Effect of Diet and Nutritional Supplements in the Management, Prevention, and Control of Inflammatory Bowel Disease: A Simple Literature Review

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### ABSTRACT

**Background:** Inflammatory bowel disease (IBD) is known for its episodic relentless course of gastrointestinal symptoms. There are two major clinically defined forms of inflammatory bowel disease (IBD), Crohn's disease (CD) and Ulcerative colitis (UC). It's associated with chronic remittent or progressive inflammatory conditions that may affect the entire gastrointestinal tract and the colonic mucosa, respectively. A lot of literatures have been done to assess the role of diet in IBD management, prevention, and control, as a result, we will review the articles that investigated the diet role in IBD, and clarify the new progress that have been done, which will help the patients and the physicians in managing, and prevention of the acute attacks.

**Objectives:** In this paper we aimed to present the role of diet and nutritional substances in the management and prevention of inflammatory bowel disease.

**Methods:** PubMed database was used for articles selection, and the following keys used in the mesh ("Crohn Disease"[Mesh]) AND ("Colitis, Ulcerative/diet therapy"[Mesh] OR "Colitis, Ulcerative/prevention and control"[Mesh] OR "Colitis, Ulcerative/therapy"[Mesh]) AND "Inflammatory Bowel Diseases"[Mesh].

**Conclusion:** patients with IBD should increase their fiber intake in their diet, and take vitamin D supplement. Also, introduction of eicosapentaenoic acid (EPA) in a free fatty acid form (EPA-FFA) into their diet is helpful. However, the overall benefit of diet in this prevalent disease still need more research looking into the variable dietary regimens that can be given in this special population.

**Keywords:** Diet, Nutritional Supplements, Management, Prevention, Control, Inflammatory Bowel Disease.

### INTRODUCTION

Inflammatory bowel disease (IBD) is known for its episodic relentless course of gastrointestinal symptoms. It's a chronic and progressive inflammatory condition that may affect the entire gastrointestinal tract and/or the colonic mucosa, respectively, and is associated with an increased risk for colon cancer. Crohn's disease (CD) and ulcerative colitis (UC) are the two major forms of the disease, and have been associated with systemic clinical manifestations causing great distress to their patients<sup>(1)</sup>. IBD aetiology could not be proven with one single reason, but it has been appreciated to have a genetic basis and likely involves a response of the immune system to some environmental agents. The discordance of IBD among different factors, such as monozygotic twins<sup>(2)</sup>, the development of IBD in immigrants to high-prevalence countries<sup>(3)</sup>, and in countries undergoing rapid westernization also highlights the importance of environmental factors in this disease pathogenesis. Moreover, a controlled diet would aid in alleviation of the symptoms, sustain quality of life and people with vitamin D deficiency were not associated with development of IBD<sup>(4)</sup>. On the other hand, certain food types are common triggers for exacerbation of IBD symptoms, and low fruit

consumption has been linked to higher rate of IBD in Saudi Arabia<sup>(5,6)</sup>. Therefore, a lot of literatures have been done to assess the link between diet and IBD in terms of aetiology, management, prevention, and control. The objective of this paper is to present the role of diet and nutritional substances in the management and prevention of inflammatory bowel disease.

### METHODS

PubMed was chosen as the search database for the articles selection, because it is one of the major research databases within the suite of resources that have been developed by the National Center for Biotechnology Information (NCBI). The following keys used for the Mesh(("Crohn Disease"[Mesh]) AND ( "Colitis, Ulcerative/diet therapy"[Mesh] OR "Colitis, Ulcerative/prevention and control"[Mesh] OR "Colitis, Ulcerative/therapy"[Mesh] )) AND "Inflammatory Bowel Diseases"[Mesh] A total of 3604 articles were found, with further restriction by PubMed filters, and reviewing the articles titles and abstracts the final results were 10 articles. In regards to the **inclusion criteria**, the articles were selected based on the relevance to the project which should include

one of the following topics, confirmed Inflammatory Bowel Disease case, diet effect on IBD patients, IBD management and control, and human patients.

**Exclusion criteria** were all other articles which did not have one of these topics as their primary endpoint, or repeated studies, and systematic reviews or meta-analysis. Further applying these criteria, we excluded five articles (two of them were systematic reviews, one study was meta-analysis, one study was done on rats, and another one was about biological markers). No software was used to analyze the data. The data was extracted based on specific form that contain (Title of the study, name of the author, Objective, Summary, Results, and Outcomes), these data were reviewed by the group members to assess the relation of cholelithiasis to bariatric surgery, and weigh the pros and cons of prophylaxis measurement use. Double

revision of each member's outcomes was applied to ensure the validity and minimize the mistakes.

**RESULTS**

From the eligible 5 studies, 3 of them were randomized control trials and two of them were prospective studies. All of them had IBD patients in their sample and only one of the clinical trials had healthy patients included in the sample. All of the studies had some form of diet therapy which ranged from iron and vitamin D to synbiotics. We assessed the risk of bias in the clinical trials and all were low risk of bias. However, one study was not blinded but the rest were double-blinded. The studies characteristics can be further seen in Table 1. Table 2 included the characteristics of the study samples and genders included.

**Table 1:** eligible 5 studies, 3 of them were randomized control trials and two of them were prospective studies.

Study (Year)	Study Design	Country	Intervention	Duration of Intervention	Impact on IBD	Ref.
Scaioli et al. (2015)	Clinical trial	Italy	EPA-FFA (n-3 PUFAs)	56 Days	Intake of EPA-FFA increased Plasma n-3 PUFA in IBD patients with clinical and statistical significance	(7)
Pappa et al. (2014)	Randomised Controlled Trial	USA	Vitamin D2	12 Month	Lower incidence of elevated inflammatory markers with higher vitamin D dose	(8)
Ahmed et al. (2013)	Randomised Controlled Trial	UK	Synbiotic	2 Month	No significance in disease activity and micro-flora	(9)
Ananthakrishnan et al. (2013)	Prospective	USA	Fibers	Years	Long-term intake of dietary fiber is associated with lower risk of CD in women	(10)
Lupa A et al. (2015)	Prospective	Romania	Iron	17 Month	(53.3%) of IBD patients had iron deficiency	(11)

**Table 2:** included the characteristics of the study samples and genders.

Study (year)	Total Participants	(%) CD	(%) UC	(%) Healthy Participants	Gender of Participant	Ref.
Scaioli et al. (2015)	35	(28.5) 10	(28.5) 10	(42.8) 15	Both	(7)
Pappa et al. (2014)	63	(58.7) 37	(41.26) 26	(0) 0	Both	(8)
Ahmed et al (2013)	16	(50) 8	(50) 8	(0) 0	Both	(9)
Ananthakrishnan et al. (2013)	607	(44.3) 269	(55.6) 338	(0) 0	Females	(10)
Lupa A et al ((2015)	291	(39.5) 115	(60.48) 176	(0) 0	Both	(11)

In **Scaioli *et al.*** <sup>(7)</sup>, the introduction of eicosapentaenoic acid (EPA) in a free fatty acid form (EPA-FFA) in both IBD (10 with CD and 10 with UC) and healthy patients (n=15) was done, then they measured its effect on both populations by measuring plasma long-chain n-3 polyunsaturated fatty acids (n-3 PUFAs) and red blood cell (RBC) membrane at different intervals (at the start, after 2 weeks, after 4 weeks, and after 8 weeks). At baseline, the plasma n-3 PUFA content in IBD patients was significantly higher in healthy patients (P value <0.01). However, the RBC n-6 PUFA content in IBD patients was significantly higher than healthy ones (P value <0.01) and there was no clinical significant difference between CD and UC patients. After the introduction of intervention, the change in plasma PUFA profile occurred rapidly, being evident after only 2 weeks with increase in n-3 PUFAs (around 12%) and a concomitant decrease in n-6 PUFA (around 9%) this change was 0. On the other hand, changes in the RBC membrane PUFA profile occurred slowly and progressively up to 8 weeks (2%, 5%, 9% by 2,4,8 weeks respectively) this change was significant (P value was <0.001, 95% CI, 4.1 -3.7 to 4.4-). However, There were no significant differences in PUFA content between healthy patients and IBD patients at the end of the study, this was explained in the study by comparable incorporation, by inference and absorption in both groups <sup>(7)</sup>. **Pappa *et al.*** <sup>(8)</sup> studied the maintenance of vitamin D status in children and adolescents, affected with IBD, aged eight to eighteen years. This non-blinded trial had (total sample n=63, CD n=37, UC n=26), and compared two supplementation regimens of vitamin D with regards to efficacy and safety in maintaining optimal 25OHD in children with IBD. Only forty-eight participants from the original sixty-three completed this trial. The daily oral doses of 2,000 IU were inadequate in maintaining serum 25OHD concentration. Lower Incidence of elevated inflammatory markers and cytokines in participants who took a higher dose of vitamin D2, this merited further study. **Ahmed *et al.*** tried to test the effect of oral synbiotic in alteration of the fecal microflora, and disease activity in IBD patients. This RCT was a crossover study between the synbiotic and placebo with 1 month each for both groups (total size n=16, CD n=8, UC n=8). The disease activity was assessed via Harvey Bradshaw Index (HBI) and no significant difference was noted between the groups. The fecal microflora as well did not significantly change by the end of the study and the researchers attributed these results to the small size and short duration of the study <sup>(9)</sup>. In **Ananthakrishnan *et al.*** the increase of dietary fiber effect on the reduction of IBD risk was studied with prospective study. The sample included (total sample n=170,776, total patients n=607 -CD

n=269, UC n=338-) whom were all females. The study compared the risk of IBD between the lowest quintile (average 11 g/day) of fiber intake with the highest quintile (average 25 g/day). Women in the highest quintile of fiber intake had a significantly reduced risk of CD (P value 0.08, HR, 0.59, 95% CI, 0.39–0.90), but there was no statistically significant association between the intake of dietary fiber and UC (P value 0.41, HR 0.82, 95% CI, 0.58–1.17). the strongest effect of total fiber intake for ileocolonic CD (HR, 0.47; 95% CI, 0.22–1.00) specially ileal involvement (HR, 0.50;95% CI, 0.29–0.86) compared to colonic (HR, 0.62; 95% CI, 0.38–1.01)<sup>(10)</sup>. **Lupa *Aet al.*** sought to determine the prevalence of anemia and iron deficiency in Romanians affected with IBD. This prospective study of multicenter involvement included (total sample n=291, CD n=115, UC n=176) of the Romanian people of both sexes and aged above eighteen years. The prevalence of anemia was (31.3%), with an alarming (53.3%) of all IBD patients having iron deficiency. Around a third of these IBD patients had anemia<sup>(11)</sup>.

## DISCUSSION

This review article was conducted to assess the effect of diet in the management, prevention, and control of inflammatory bowel disease. Searching into the PubMed database with the MESH words described above, and after applying our exclusion and inclusion criteria we ended up with five eligible articles. The strength of this study were in all studies included both genders except for one which studied female participants only<sup>(10)</sup>. All studies included adults with the exemption of one study in children and adolescents<sup>(8)</sup>. The ranges of interventions included were: iron, vitamin D, fish oil, fibers and synbiotics. All studies were within the recent five years. Analysis of these articles, which included three clinical trials and two prospective studies, along with systematic reviews are presented herewith.

## Reviews

A systematic and meta-analysis review in 2017 by **Derwaet *al.*** studied the efficacy of probiotics in inflammatory bowel disease in twenty-two RCTs. It showed that while probiotics appeared to be safe in IBD patients, they might also play a role as an alternative to UC maintenance treatments <sup>(12)</sup>. A systematic and meta-analysis review in 2017, studied the efficacy of probiotics in inflammatory bowel disease in twenty-seven RCTs. It showed that probiotics appeared to be safe to use in IBD patients, they also may play a role in attaining an effective remission in both spectrums of the disease and even in children as well<sup>(13)</sup>.

### Clinical trials

One blinded clinical trial sought the maintenance of vitamin D in children and adolescents. It showed that inflammatory markers were reduced following a higher intake of vitamin D2 in participants. This study could be applied to adults as well in further research<sup>(8)</sup>. In one randomized trial, testing of oral synbiotics in alteration of IBD activity and fecal microflora concluded that there was no significant difference, as the fecal microflora and the Harvey Bradshaw Index (HBI) remained unchanged<sup>(9)</sup>. This study required a larger sample size and longer intervention duration. Another clinical trial tried to study the effect of EPA in a free fatty acid form on plasma n-3 PUFA and its RBC membrane ratio as well. At the start of the trial, the healthy patients had higher levels. And they initiated the dietary intervention which increased the levels of n-3 PUFA in plasma and red blood cells membrane at the end of the 8 weeks. Moreover, the healthy patients showed increase in n-3 PUFA with no significant difference between the two groups at the end of the study<sup>(7)</sup>.

### Prospective studies

Another study included the largest sample of IBD patients in this review. It showed that increased intake of dietary fiber significantly reduced the risk of Crohn's disease in females in the USA<sup>(10)</sup>. This study should be done in males and include the pediatric age group to better benefit the IBD populace. In a recent prospective study on Romanians with IBD, an alarming rate of more than half of the sample had iron deficiency<sup>(11)</sup>. This finding should alert further research to take into consideration anemia in IBD patients and appropriate iron supplementation.

### Limitations

We acknowledge the limitations we had in this study. We could not find more articles with the outcome criteria for inclusion into our review. No studies were included on the effects of fiber diet on children and adolescents to ascertain if it was effective in this population.

### CONCLUSION

In our review, we included five research articles and two systematic reviews and meta-analysis, all papers had inflammatory bowel disease patients of both Crohn's disease and ulcerative colitis. Fiber diets, especially ones containing fruit, should be given in long periods to patients with IBD. Vitamin D supplements should be given in high quantities to children and adolescents affected with

IBD. Moreover, EPA in a free fatty acid form is recommended in these patients since they have lower value of n-3 PUFA compared to normal patients. The overall benefit of diet in this prevalent disease still need more research looking into the variable dietary regimens that can be given in this special population. More clinical trials would be needed to give a final judgment on this topic but the review we done shows promising results regarding the topic.

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