INFLAMMATORY BOWEL DISEASES AND NUTRIGENOMICS: IMPORTANCE, PREVENTION AND TREATMENT: A REVIEW

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ABSTRACT

Inflammatory bowel diseases (IBDs) are chronic illnesses that affect not only the gut and gastrointestinal tract, but also the extraintestinal organs in many people. The primary reasons for this are changes in diet, genetic makeup, and environmental factors. The gradually changing diet is increasing the risk of the disease and increasing its severity. The immune system of the gut is affected, and the risk of the disease increases by increasing the permeability of the mucosal layer. The dietary changes interfere with the immune system, and the disease accelerates. The dietary pattern and the micronutrients are reviewed to understand the treatment procedure. Later, future interventions are considered for the treatment of inflammatory bowel disease. The genetic makeup of humans also plays a significant role in the development of this disease. Heredity also plays an important role in the inflammation of the gut. Many treatment procedures and recent studies have found many resolving issues to prevent inflammatory bowel disease. The genetic makeup cannot be changed, but the microbiome can be modified accordingly to prevent the inflammation of the gut. This review examines the role of nutrition, genetics, and phytonutrients in IBD treatment.

Keywords: Crohn's disease, Genome, Gut, Inflammation, microflora, nutrition, Pro and Prebiotics.
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1. INTRODUCTION

Crohn's disease (CD) is an inflammatory bowel disease (IBD) that can affect any part of the digestive system (from mouth to anus). Malnutrition affects 65-75 percent of CD patients, and it is now widely accepted that diet is critical in the disease's management[1].Nutrigenomics identifies interaction between gene and diet. It shows how the diet influences the genetic variations and gene regulation in an individual. Nutrition is the science which encompasses the intake of food which consists of nutrients in required quantity, facilitating proper

development and growth of an individual [2, 3].There has been a growing interest in nutrition as a critical factor in CD treatment over the last few years. Scientific research on the impact of diet on gut health has been fueled by an increased awareness of the effects of the environment on disease pathogenesis, as well as a better understanding of the microbiome and its functional role[2, 3].

Nutritional requirements are influenced by genetic variation in a variety of ways. Nutrition, especially intake of good quality nutrition varies from person to person [1-7]. For one-person, good nutrition may not be as beneficial as it is for another. Nutrigenetics is a term that refers to the relationship between diet and genotype. It focuses on the effects of nutrition on gene regulation and protein expression in general. To learn more about the genome's functional composition, advanced technologies are very useful and innovative[4]. Also, nutrigenetics provides information on gene regulation and expression. Nutrigenetics and nutrigenomics go hand in hand, meaning they are similar in some ways. Both allow for a better understanding of the role of evidence-based intervention strategies in maintaining good health as well as delaying diet-related diseases [9, 10]. It determines different nutrient requirements for various genotypes. A change in the patient's diet can often aid in the stabilization of the disease. Understanding the mechanism by which nutrition influences gene and protein expression levels aids in analyzing the influence of dietary components on cellular metabolism and organism metabolism. Microarrays or NGS are essential for this purpose because both have their advantages and disadvantages. The basic etiology and nature of Crohn's Disease are better understood thanks to nutrigenomics[5, 6].

IBD refers to two idiopathic pathologies: Ulcerative Colitis (UC) and CD. They are immunologically mediated chronic progressive disorders that primarily affect the mucosal lining of the colon and, in some cases, the entire GI tract. The pathogenesis of IBD is due to a dysregulated interaction between the intestinal microbiota and the mucosal immune system, with environmental factors influencing the onset and recurrence of the disease [6, 9]. They include shifts in the proportions of Bestrides and Firmicutes, as well as a decrease in Clostridiales as the percentage of Gamaprobacteria and Enterobacteria rises. In patience with Crohn's disease, there is an increase in *Candida albicans.* In this review, We would like to highlight some of the most recent nutrition research findings for the treatment of IBD.

Method

A literature review was conducted by systematically synthesizing published studies identified through bibliographical searches per-formed in electronic databases; Ovid Medline, CINAHL, Scopus, and PubMed from database commencement until 1 March 2022.The search criteria included combinations of the following search terms and keywords: FODMAP*,"low FODMAP", "Fermentable oligosaccharide*", fructo*,"irritable bowel syndrome*", IBS. No language or date restrictions were applied. No restrictions were placedon study design, with reviews and commentaries included. Articles were reviewed for clinical studies focusing on predictors of response, implementation of diet, long-term effects of the low FODMAP diet in patients with IBS. Reference lists of the included articles were also reviewed.

Diet andIBD

Diet influences microbial composition, intestinal barrier integrity, and host immunity. Changing your diet may cause gut dysbiosis, altered gut barrier, immune activation, and tissue damage, which can lead to IBD[7]. Inflammatory bowel diseases are often caused by poor diet and a sedentary lifestyle.IBD may be aggravated or even accelerated by a diet high in saturated fats and red meat, as well as refined sugars[8]. It's difficult to pin down the role of a single food in any complex disease where diet is a contributing factor because dietary patterns involve exposure to various food groups. There isn't enough evidence to say whether

diet affects IBD activity right now[9]. Frequent diarrhea, bleeding ulcers, hematochezia, stomach cramps, bloating, growth retardation, and other complications are common in IBD patients. Dietary nutrition and genetic factors both play a role in the development of such conditions[10].Patients with IBD may suffer from malnutrition because of self-imposed restrictions on certain foods to manage their symptoms. Malnutrition, which includes protein-calorie malnutrition, micronutrient deficiency, or both, can affect up to 85% of patients with IBD[11]. Iron, cobalamin, folic acid, vitamin A, vitamin D, vitamin K, selenium, zinc, and vitamin B1 are the most common micronutrient deficiencies in IBD patients[11]. Food consumption is a cultural and social activity, as well as a source of pleasure and conviviality with others, in addition to its biological role. In people with IBD, these critical psychosocial roles may be altered[12]. Patients with IBD may avoid dining outside the home or do not share the same menu or diet with other household members because of their eating habits. Furthermore, malnutrition is common in anorexia nervosa (AN) and especially in Crohn's disease patients[13], affecting up to 70% of patients with active IBD and up to 38% of patients in remission.

Dietis important in redressing the balance between microbial challenge and the host response because it has been implicated in several inflammatory diseases and conditions, including type II diabetes mellitus, cardiovascular diseases, rheumatoid arthritis, and inflammatory bowel disease, all of which have also been associated with periodontal diseases[14]. Based on the pathology of periodontal disease, the assumption is that specific nutrients which can modulate immune and inflammatory responses could in turn modulate periodontal health.

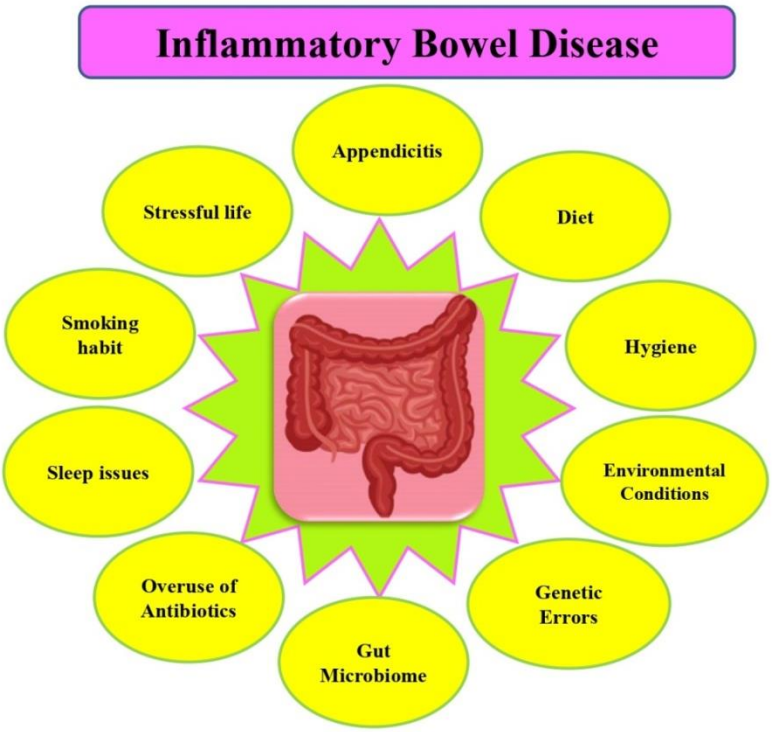


Figure 1. Factors that contribute to the development of IBD

The IBD is very common in both children as well as adults. The nutrition guidelines differ with the age, but it does not differ with the population guidelines [18]. Some nutrients like Vitamin D, certain phytochemicals, and long chain omega 3 polyunsaturated fatty acids are needed at a higher level. Use of prebiotics as well as probiotics might also help. Nutrient optimization helps in preventing the disease rather than curing the symptoms, since its occurrence is mostly genetic [15, 16]. IBD can be divided into two categories based on the way the disease manifests itself and where it occurs. The etiology and treatment procedures for each of these conditions are outlined in the following sections, as are their respective causes [12, 18]. Complex genetic and environmental factors play a role in the etiology of these IBDs, including the gut microbiota, which are susceptible to interaction. Single nucleotide polymorphisms (SNPs) have been linked to a wide range of diseases by genome-wide association studies [39, 41]. A diet and specific interventions based on a gene's involvement, together with the environment's characteristics, are necessary to achieve the desired outcomes. Epigenetics and gut microbiota interactions have a direct impact on the efficacy of dietary interventions.

Nutrigenomics and IBD

Nutritional genomics has the potential to transform dietary guidelines and personal recommendations in the future (Figure 3) [15]. A major objective of nutritional genomics is to determine how genetic variation affects the diet-disease interaction. This is accomplished through nutrigenomics, which studies how nutrients affect the genome, proteome, and metabolome. Nutritional genomics also includes nutrigenetics.The primary objective of nutrigenetic research is to determine how genetic variation affects the relationship between diet and disease. Because it has been used for decades to study rare monogenic diseases like phenylketonuria, nutrigenetics may one day help prevent common multifactorial disorders decades before they manifest clinically by providing a basis for individualized dietary recommendations based on genetic makeup.

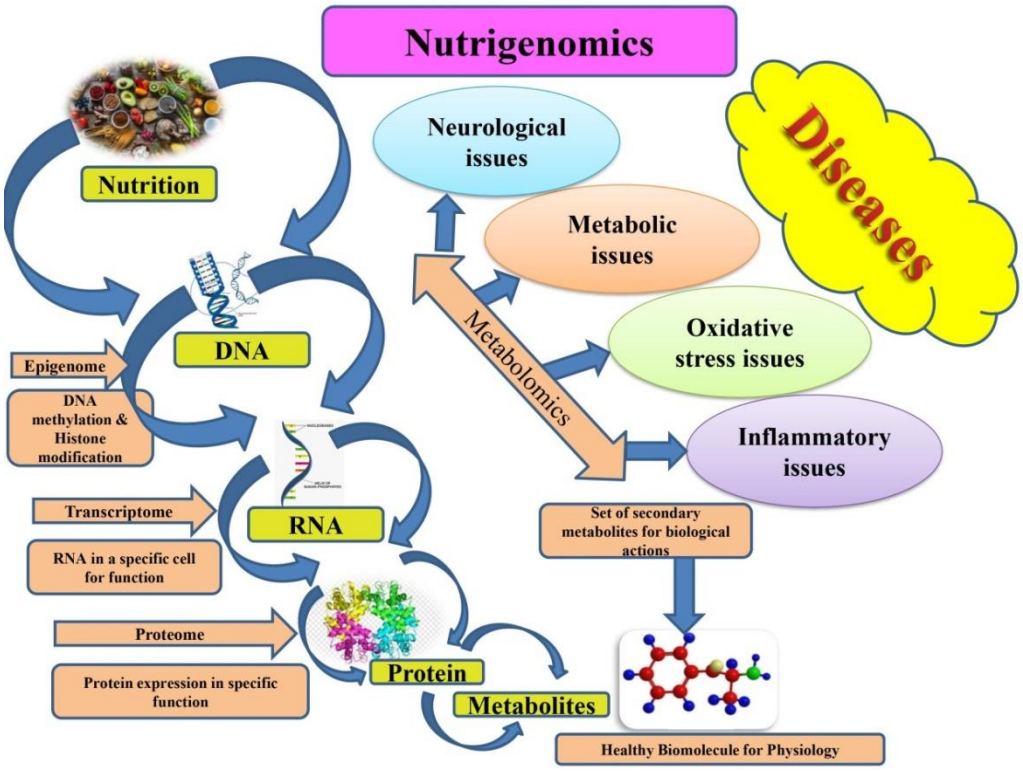


Figure 2. Nutrigenomics importance in combating inflammatory bowel disease (IBD)

Nutritional patterns and the type and quality of the nutrients consumed in the diet can cause or worsen the condition of IBD in people who are already suffering from it[20, 21].Nutritional aspects that can help prevent IBD include

- prevent malnutrition
- therapies involving better nutrition
- knowledge of dietary components leading to IBD and components which ameliorate the symptoms of IBD

IBD alters the gut microbiota in addition to other aspects of health. Inflammatory bowel disease can be alleviated by the microbiota's ability to produce omega 3 fatty acids and PUFAs. [23, 24] Inflammatory cell production is reduced by omega 3 fatty acids like eicosapentaenoic acid (a polyunsaturated fatty acid found especially in fish oils) and docosahexaenoic acid [23, 24]. Lipoxins are formed when PUFAs alter membrane function, inflammation is reduced because of this.

Role of genome

The human population makes a significant contribution to the disequilibrium. Closely located alleles can become separated from each other in this way. Based on such events, genome-wide studies are being conducted [20, 18]. It identifies the genetic markers that are responsible for any phenotypic characteristics. Large-scale genome-wide association studies have identified more than 200 genetic loci linked to IBD over the last decade, some of which are also linked to other chronic autoimmune diseases. Apart from major European risk variants like *NOD2* (the first identified mutation that mediates immune response to gut bacteria) and *IL23R*, which are not present in east Asians, many loci are shared across ancestral groups[16].In comparison to children of non-immigrants, epidemiological studies of migrant populations have found that the offspring of individuals migrating from Asia to the developed world have a similar high incidence of IBD, indicating that risk may be triggered by earlier life exposure to environmental antigens[17]. In other study by Jostins *et al*.[18],related that the susceptibility loci for the IBD have a significant overlapping with the loci of susceptibility for mycobacterial infections. This led to a greater ability to understand the causes through investigation of different clues and evidence from the disturbed pathways present in the intestinal immune system. An important transcriptional regulator for intestinal inflammation is the NF-κB [12, 15, 18].It is responsible for the integrity of the epithelium and maintaining the mucosal immune homeostasis. In IBD, post-translational modifications like, ubiquitination generally fails to take place. The activity of NF-κB is mostly dependent on the ubiquitination modification. The malfunctioning of the NF-κB gene results in the susceptibility of inflammatory bowel disease. A gene for RORC was identified on the chromosome 1q21, which enhances susceptibility towards both the forms of IBD. RORC is RAR-related orphan receptor C, is a type of nuclear receptor. It helps in the differentiation of naïve $CD4^+$ T-Cell. They help in the production of IL-17 [19, 21]. Excessive immune response is restricted by a signaling pathway carried out by the $TGF\beta$. Through this signaling pathway, collagen synthesis is induced in the gastro-intestinal tract. It acts as a potent profibrogenic agent. 12 loci which had the gene for this signaling pathway was identified. The degradation of $TGF\beta$ influences both the types of IBD. The number of loci keeps on increasing and as well as the susceptibility.

Role of nutrition

Nutrition is the organic process by which an organism assimilates food and uses it for growth and maintenance, whereas a nutrient is a source of nourishment, such as food, that can be metabolized by an organism to provide energy and build tissue. A person's diet must contain both "macronutrients" (such as fats, carbohydrates, and proteins) and "micronutrients," which include trace minerals, vitamins, amino acids, and polyunsaturated fatty acids (PUFA) [16, 18].The recommended daily nutrient intake plays a significant role in management of IBD. Nutritional intake has a significant impact on the gut and its lining, preventing

inflammation. When the interleukin gene is mutated, inflammation results, which has a wide-ranging effect on the microbiota.

Dietary lipids are considered as static metabolic reserves of energy. They play a major role in signal transduction by acting as the main component of the transduction pathway. They also modulate the inflammatory responses in the host and enhances both promotion and resolute. They implicate pathogenesis, of the inflammation of the intestine which results in inflammatory bowel disease. The mucosal immunity is affected too. There are variable results in relation to the peroxisome proliferator-activated receptor (PPARG) genetic variants (Pro12Ala and C161T) with IBD. In the studies of Hume et al., reported there is no association IBD with Australian cohort [45].] Shrestha et al. studies exhibited positive relationships of IBD in Chinese not in a Dutch population [60]. Whereas the Pro12Ala genetic variants can be found protective against the population of European Caucasians in Crohn's disease (CD) as newer developments. Ethnic differences are shown to be associated with phenotypic variation as supportive and useful characteristics in studies on ethnic differences. Dietary factors, such as lipid-rich, high-fat foods, play a significant role in the development of IBD (references)

Lipids such as linoleic acid (conjugated) have been shown to have immunomodulatory activity in patients with active CD issues, which is aided by the modulation of Peroxisome proliferator-activated receptor gamma (PPARG) variants. In other findings of Ferreira et al., on CD cohort in Caucasian ethnic exhibited result due to intake of high fatty molecules like total, saturated and monounsaturated foods with the ratio of n-6/n-3 PUFAs were higher in the association of active phenotype. The study also reported for the 4 genetic polymorphisms, in that two are considered for the IBD like PPAR-g SNPs 161C/T and Pro12Ala SNPs with the control population. These SNPs were also found to have no significant effect on disease influence, which could be due to the SNPs' presence or a higher trans-fat food intake in their diet as a negative effect. [55, 60]

Role ofMicronutrients

The micronutrients play a major role in the wellbeing of the gut especially the intestine. They help nourishing the gut and maintain the health of the intestine. It works along with the microflora of the gut and maintains the gut health. Many review reports on requirement vitamin and mineral for the genomic stability maintenance, with regards to the impact of the micronutrients in the genomics project [36, 60]. Micronutrients are essential nutrients that may be required for the CD at a higher level than usual, and their utilization will be linked to immune activity and inflammation response control. Other research has focused on the importance of minerals in the correct form, as well as the need for sufficient selenium based on genotypic characteristics. [66, 65].

Vitamin D is a critical nutrient that patients with CD require in greater amounts than expected. [65, 68]. Jostins et al.,[18] reported that Vitamin D is linked to IBD because of genetic requirements, and SNPs are involved in vitamin D intake and distribution, which leads to immune-chip activation. Inflammatory processes have been specifically linked with available microbiota and their well-known genes. In the presence of Clostridium difficile in gut found to be increased level of plasma vitamin D association to reduce the risk of IBD [25, 26], whereas decreased level of vitamin D circulation increased the risk of inflammatory diseases and types of cancer [36, 40].

Malnutrition is common in CD patients, identified by severe oral inflammation with loss of taste, chewing, and swallowing difficulties. This indicates which foods should be avoided, such as tomatoes, which act as acidifiers in CD. CD revealed that 8 to 29% of people in the oral issues had some form of disease activity [16]. A common oral symptom is labial swelling, which is also known as gingiva and mucosa layer swelling.

Food intolerance

Many studies show that restricting FODMAPs (fermentable oligo-, disaccharides, mono-, and polyol-containing carbohydrates)

improves symptoms in between 50% and 80% of people with irritable bowel syndrome (IBS)[19]. An approach to dietary therapy for IBD that considers food intolerances linked to specific genes and their FODMAPs can be helpful. There is a correlation between food intolerance and a particular gene or variation in genes. Generally, foods high in FODMAPs are safe for healthy people; those who have recently experienced inflammation and have difficulty absorption due to an overdose of food exhibit laxative properties and fermentation by the bacteria occurs [72]. Other type of food intolerance like brassicavegetables, cooked tomatoes, mushrooms, mustard, sweet potatoes, wasabi raw, sulphur dioxide, sulphites and sulphur compounds also exhibit link with genotype of IBD.

Low FODMAP education can be delivered and evaluated using digital applications on smartphones. 83% of US dietitians[20] recommend patients download nutrition and health apps, and 84% of dietitians in a three-country study conducted in Australia, New Zealand, and the United Kingdom also recommended patients to download nutrition and health apps. Monash University Low FODMAP Diet was the second most frequently recommended or self-initiated nutrition app in this study, according to the authors. Using the Mobile Nutrition Care Process Grid[21], dietitians have a framework for using apps in their practice. A low FODMAP diet taught to patients through the internet, or an app has not been thoroughly tested, so it cannot be recommended at this time.

Probiotics and Prebiotics

Probiotics are bacteria that can survive in the stomach acid and make it to the small intestine and colon. They provide health benefits to the gut and colon as a host. Adding probiotics to your diet can have an antimicrobial effect and improve your body's ability to fight off disease-causing microorganisms. Prebiotics, which are dietary compounds that nourish commensal bacteria, were found to have no effect on CD activity index, endoscopic score, or immunohistochemistry [1].Table 1illustrates examples of certainprobiotics and with respective functions.

Table 1: Significance of probiotics in inflammatory bowel diseases

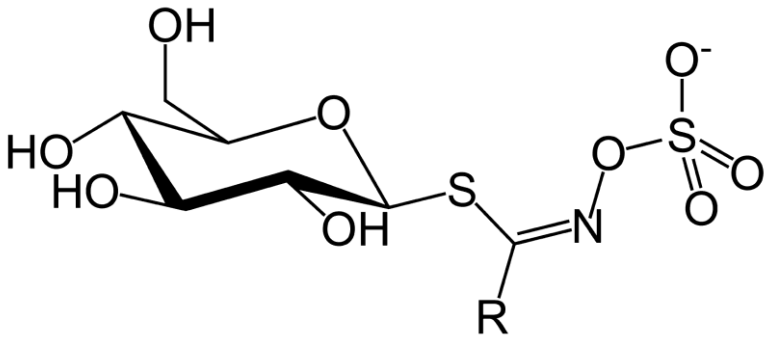
Probiotic	Effect on the gut
Escherichia coli	T cell expansion into the mucosa is down regulated.
Saccharomyces boulardii	Infiltration of T-cells into the mucosa in restricted.
Clostridium butricium	Short chain fatty acids are secreted.
Helminthes	Restricts immune respond towards helper T-cells.
Lactobacillus	Restriction of nuclear translocation, degradation of interleukin.

In IBD, microbiota diversity has been shown to play an important role in the predictive module for therapeutic approaches [48, 50]. It's also been suggested that a specific number of intestinal microbes may play a role in IBD [55, 60]. Fecal transplantation is one of the therapies for IBD, and it has been widely acknowledged that, in the long run, such therapy will not be a viable option [50, 52]. Furthermore, many concerns have been raised about the efficacy of the treatment. Controlling the gut microbiota through diet may be a viable option for achieving efficacy in a long-term strategy. The importance of diet in modulating the gut microbiota has been well documented [60, 62, 70]. Vitamin D, for example, is important in the treatment of IBD [55, 56]. Probiotics have already been defined by the FAO/WHO as "live gut microbiota confer that a fixing health issues by the host when taken in sufficient amounts of such nutritive foods." The combination of prebiotics and plant products allows for a responsive modulation of colony in the gut

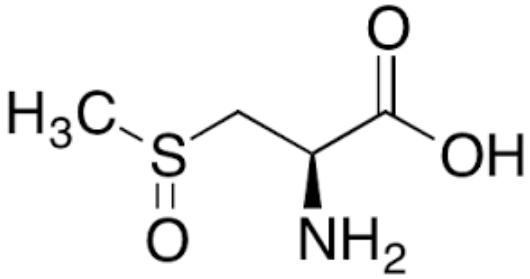
microbiota, which may be particularly beneficial to patients [42, 50, 65]. Probiotic bacteria in the gut are thought to produce conjugated linoleic acid, which is involved in suppressing IBD disease via the PPAR-gamma target [25, 34]. Prebiotics are easily digested and fermented into fatty acid short chains, which affect the growth and support of certain beneficial bacteria in the gut [16, 22].

Phytonutrients and IBD

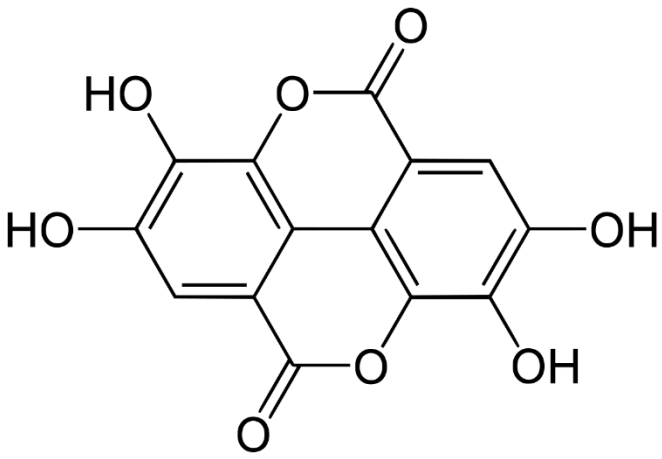
Polyphenolic compounds are one of the most important secondary metabolites in higher plants[27].Polyphenolic compounds play a key role in Crohn's Disease or IBD susceptibility. Many of them influence the inflammatory response, particularly in cases where the genes are ineffective. Sulphur-containing phytochemicals can be found in vegetables such as cauliflower, cabbage, and broccoli (Figure 4). In CD patients, they have a polarizing effect [22, 27]. Using 10 of the most common edible foods in the listed group, Laing et al. reported for SNPs and their association with either beneficial or harmful effects [27, 28]. In this context, one of the SNPs was strongly linked to negative effects on immune response in patients who expressed one of the major CD groups [27, 29]. Hydrolysable tannins are found in some fruits and nuts, and their compounds are ellagic acid and ellagitannins. These compounds were studied in vitro in genetically modified cell experiments and found to have a significant contribution and potential for reducing inflammation [42, 44].



A. Glucosinolate



B. S-methyl cysteine sulphoxide



C. Ellagic acid

Figure 4. Sulphur containing phytochemicals

Factors affecting IBD This section in Table format

IBD has an etiology that is yet unidentified. Inflammatory bowel disease can be caused by a variety of factors. The following are some of them:

1. **Hereditary**
2. **Genetic** - The majority of very early onset of IBD are caused by genetic defects. The difference in the genetics causes this disorder that has affects in gene function. These are very rare in allele frequency. With recent technology in genetic mapping and sequencing techniques importance of these rare disorders. [51, 53]

   50 genetic disorders are identified and associated with IBD such as immunopathology.
3. **Environmental** – The way we live may affect the chances of developing IBD and it is more common in developed countries. Factors like infection, smoking, stress, air and water pollution, diet, also food additives have been examined in IBD. These affects health in humans in various types [25, 39].

   Cigarette smoking was the earlier environmental cause. Putative mechanisms where smoking exerts the immune system in Ulcerative colitis involves in the reduction in tumor necrosis factor production i.e. TNF alpha *through the* action of nicotine, increases the production IL-10 to carbon monoxide in cigarette smoke that increases the synthesis of mucin and decreases in IL-8 expression [26, 65]. Also the higher amount of carbon monoxide from smoke that cause impairment in vasodilation capacity.
4. **Diet** - Diet influences the intestinal inflammation *through many* pathways, such as, gut-altering microbiome, affects the intestinal barrier affecting permeability and directs the effect of constituents that acts as food antigens [36, 55]

Consumption of high-fat diet can affect the dextran sodium sulfate-induced colitis in mice. Also, it alters the bile acid composition.

High intake of dietary fiber, especially fruits and Brassica vegetables decreases the risk of CD, but not UC. Food antigens acts as important stimuli that leads to the pathogenesis of IBD. [25, 53].

Food additives such as Aluminum, titanium dioxide, and small particles are implicated in murine models of colitis.

5. **Stress**- Stress is defined as a lack of harmony or threatened homeostasis. The hypothalamus-pituitary-adrenal axis and the immune system, these two works together when the body is in stress. HPA axis is activated by producing cytokines that results in the production of powerful anti-inflammatory agents i.e. glucocorticoids [13, 26, 53]

TYPESOF INFLAMMATORY BOWEL DISEASE

Inflammatory bowel disease is a term that is used to explain the chronic inflammation of our digestive tract. [52, 58]. Following are the types:

i). Ulcerative colitis

This is a condition that are involved in any type of inflammation and sores that causes any sort of pain in the body along the superficial lining of the large intestine and rectum.

Causes

The development of the disease is multifactorial. Patients have mucosal inflammation that is a burning sensation starting in the rectum continuing to proximal segments of the colon. It affects the adults aged between 30-40 years of age that results in disability [9, 25]. Most of the causesare due to the malfunction of immune system. Any infections as defensive immune system will try to fight against invasions, may be abnormal activity failure to response by the immune system and in such condition cells of the digestive tract comes under severe infections. Smoking can be one of the causes that are associated with ulcerative colitis [55, 67].

Clinical Symptoms

- Stomach pain
- Frequent hunger
- Weight loss
- Fever
- Dehydration, soreness
- Few RBC

Treatment

The patients are said to have a strict control in disease control. Treatments can be in three types:

Diet - Patient should follow the diet minimum of 3 months until the symptoms lessens and should follow at least every 6–12 months with the goal of maintaining a tight control. A balanced diet that contains fiber, lean protein, fruits, and vegetables should provide enough vitamins and nutrients [62, 71].

Medicine - When patients have symptoms of ulcerative colitis flare, infection should be denied and sigmoidoscopy, fecal calprotectin, or stool lactoferrin should be examined.

Medically prescribed few drugs that can be:

Antibiotics - Amino salicylates - 5-aminosalicylic acid (5-ASA) that fights the inflammation and controls the symptoms.

Corticosteroids-anti-inflammatory drugs

Immunomodulators – this helps to stop the immune system attacking our colon. This may take time up to 3 months.

Loperamide-This may slow or stop diarrhea. Should be taken in doctor's consultation.

Patients are also given azathioprine or 6-mercaptopurine have active metabolite in blood concentrations and 6-thioguanine to check an adequate therapeutic amount [16, 18].

Surgery – Surgery may be needed to remove the colon or colon and rectum.

To detect dysplasia and early cancer in ulcerative colitis patients should undergo regular surveillance colonoscopy and patients with extensive colitis and left-sided disease should undergo a colonoscopy starting from 8 years after diagnosis in every 1–2 years [36, 39].

ii). Crohn's disease (CD)

In this condition, the inflammation extends from the mucosa to the serosathrough the entire thickness of the bowel wall. This is a relapsing and remitting course of disease.

Causes

The exact cause is still not known. With several relapses, this can progress from mild to moderate inflammatory conditions to severe penetrating or structuring disease [43, 46]. This may affect any part of the gastrointestinal tract. In Crohn's disease, phenotypic genetic association occurs that is

a NOD2/CARD15 mutation is associated [52, 53].

In this case immune system attacks foods, beneficial bacteria, substances.

During the attack, white blood cells build up in the lining of the gut and causes inflammation that leads to bowel injury and ulcerations. Smoking is another cause[39, 41].

Clinical Symptoms

- Fever, diarrhea
- abdominal cramps
- blood in stool
- fatigue
- weight loss
- feeling a frequent need for bowel movements

Treatment

Treatment includes medication, surgery, and nutritional diet.

Moderate diseases can be treated by oral melamine, then Immunomodulators like thiopurines, methotrexate, and steroids. Severe disease will be treated using a combination of Immunomodulators, and biologics like infliximab, adalimumab, golimumab, vedolizumab. Biologics works by targeting and suppressing the inflammation that can trigger the Crohn's flares.

Diet- Patients need high-calorie liquid formulas.

Medications–Anti-inflammatory and anti-diarrheal drugs are used.

Anti-inflammatory drugs - Two main types of anti-inflammatory drugs that are used to treat Crohn's disease are oral 5-aminosalicylates and corticosteroids.

Immunomodulators – It may reduce the inflammatory response.

Antibiotics- It reduces the drainage and heal **fistulas**, that has abnormal connections between tissues.

Surgery- In some cases removing of intestine doesn't work. So colectomy is needed where the colon is removed.

Treatment

The main aim of Inflammatory bowel disease is to reduce the inflammation that causes any signs or symptoms. The treatment needs either surgery or any drug therapy [60, 61].

Anti-inflammatory drugs – This is often the first step in the treatment. The medications depend on which part of the colon is affected. This includes corticosteroids and amino salicylates, such as melamine,), balsalazide and olsalazine.

Immune system suppressors – These drugs suppress the immune response that releases chemicals into the body that leads to inflammation.

Examples can be azathioprine (Azasan, Imuran), mercaptopurine and methotrexate.

Biologics – This is a therapy that is directed toward neutralizing proteins that causes inflammation in the body. Some can be introduced through injection or intravenous infusions.

Examples includes certolizumab, golimumab, vedolizumab, ustekinumab (Stelara), infliximab (Remicade).

The oxidized lipids play a major role as proinflammatory mediators. Although, classes of lipid mediators were discovered whose signaling actions resolves rather than promoting inflammation [32, 34]. The resolvins especially D- and E-series (trihydroxy derivatives of docosahexaenoic [DHA] and eicosatetraenoic [EPA] acids), lipoxins (trihydroxy derivatives), protectins (derivatives of DHA), nitroalkenes, and EFOX (electrophilic oxo-derivatives). The oxidized omega-3 fatty acids contain an α, β-unsaturated keto moiety, that represents the endogenous lipids and their growing field[25, 66]. The mediators work by receptor-mediated signaling pathways or by modification due post-translational events. It downregulates the inflammatory responses. These molecules are currently serving for intense research, as they are eventually representing an emerging generation of research of new drugs to treat the inflammatory diseases such as IBD.

Future projections

The future of nutrigenomic research promises to provide additional knowledge of biological function and individual response to diet. Based on the pathology of periodontal disease, the assumption is that specific nutrients which can modulate immune and

inflammatory responses could in turn modulate periodontal health.The genomic constitution is different for different people. It affects the gut health and leads to IBD. The nutrigenomics altogether plays an important role in the originating of inflammatory bowel disease. The genetic makeup and the diet play a crucial role in the inflammation of the gut. The genetic history of CD would suggest us to prepare certain useful nutrients significant than the normal population and differences in the genetics of individual patient. Such nutrient requirements will be very important during disease eruption, but it will be very crucial to slow down the progress of the disease [61, 70-72].The identifying microflora of the gut depends mostly on the diet and the genetic constitution and future will be analyzed disease systematic by the available genomic data.

Conclusion

With the advancement of studies and research on inflammatory bowel disease, it has been found that the inflammation of the gut is caused by a reduction in the immune function of the gut microbiome. A variety of factors contribute to the development of inflammatory bowel disease. The diet of the individual, as well as the genetic makeup of the individual, are the most important factors to consider. They have a cumulative effect on gut health, and any changes or discrepancies in them result in the gut's immune system becoming less effective. When it comes to disease risk modulation, diet is an important environmental factor that interacts with the genome. With a clear understanding of these interactions, it is possible to support disease prevention by optimizing dietary guidelines.

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