

How to Cite:

Tahir, M. H., Jamil, H. M. A., Lodhi, T., Mehdi, M., Ali, M., & Ullah, I. (2023). Effect of gut microbiome alteration in inflammatory bowel disease: Microbiome-based therapy for irritable bowel syndrome. *International Journal of Health Sciences*, 7(S1), 1713–1722. <https://doi.org/10.53730/ijhs.v7nS1.14405>

Effect of gut microbiome alteration in inflammatory bowel disease: Microbiome-based therapy for irritable bowel syndrome

Dr Muhammad Hamza Tahir

Medical Officer Govt Sadiq Abbasi Hospital (Civil Hospital) Bahawalpur

Dr Hafiz Muhammad Amir Jamil

Senior Registrar Bahawal Victoria hospital, Bahawalpur
Corresponding author email: dramirjamil285@gmail.com

Dr Tahreem Lodhi

Resident Medical Officer – Er Hamdard University Hospital Karachi

Dr Muhammad Mehdi

Medical Officer, Services Institute of Medical Sciences, Lahore, Punjab, Pakistan

Dr Muhammad Ali

Medical Officer, Services Institute of Medical Sciences, Lahore, Punjab, Pakistan

Dr Ihsan Ullah

House Officer, Capital Hospital CDA, Islamabad, Pakistan

Abstract---High morbidity rates are associated with inflammatory bowel diseases such as Crohn's disease and ulcerative colitis. New studies have suggested that dysbiosis may play a role in the etiology of inflammatory bowel disease, although the cause of IBD remains unknown. Several disease pathologies, such as inflammatory bowel disease, have been associated with the intestinal microbiota, a metabolic organ with multiple physiological functions. This review summarizes the present level of knowledge regarding the impact of altered gut microbiota in inflammatory bowel disease, the mechanisms by which this occurs, and the potential significance of therapeutic methods based on gut microbiota in the prevention and treatment of IBD. It has been demonstrated that directly targeting the intestinal microbiota can treat both inflammatory bowel disease and colitis in humans and animals. To characterize the core microbiome associated with IBD and the underlying pathophysiology, however, additional research employing well-designed randomized control trials and animal models is required, as there are currently insufficient data

and contradictory results from previous studies. The environment will influence the probiotic and prebiotic treatment for IBD.

Keywords---pre & probiotic, microbiome, inflammatory bowel syndrome.

Introduction

Inflammatory bowel disease is a chronic condition that affects the mucosal structure, the makeup of the gut flora, and the biochemistry of the entire body. It is categorized as a gastrointestinal (GI) ailment. Both UC and CD can be differentiated from one another based on the presence of inflammation as well as the location inside the intestinal tract¹. Intestinal bacterial dysbiosis has emerged as one of the most pressing issues facing public health authorities throughout the world over the past decade². IBD is more widespread in developed countries such as the United States, Europe, Australia, and New Zealand than it is in emerging countries like as Brazil, South Korea, and China, but it is also on the increase in developing regions such as Asia and South America. At this time, the yearly incidence rates for UC and CD in China are, respectively, 11.6% and 1.4%³. One of the most common concepts about the origin of inflammatory bowel disease is that it is caused by an overactive immune response to alterations in the gastrointestinal microbiota or pathogenic bacteria in a genetically vulnerable host⁴. It is widely recognized that changes in the gut microbiota generate intestinal inflammation, which contributes to the pathophysiology of inflammatory bowel disease⁵, however it is not clear how these bacteria contribute to the pathogenesis of inflammatory bowel disease. If these issues can be answered, it may be possible to develop more effective treatments for inflammatory bowel disease and other conditions connected to the gut flora. Because the precise origin of inflammatory bowel disease (IBD) is unclear⁶, the primary goal of treatment is to stop flare-ups and keep patients in remission. Because the condition is not treated properly, IBD has a severe impact. This therapy, although having some positive effects in the near term, invariably results in immunological tolerance being lost and drug resistance⁷. Inflammatory bowel disease (IBD) and the related problems are treated using prebiotics, probiotics, and synbiotics as a kind of complementary and alternative medicine (CAM). This is due to the fact that the therapeutic efficacy of the drugs that are now available is insufficient, and that these treatments also have considerable detrimental effects. Alterations in the intestinal microbial ecology, the illness's pathophysiology, and the therapies that are now available are discussed in this synopsis of inflammatory bowel disease.

Pathology of Inflammatory Bowel Disease and Alteration of the Gut Microbiota

The gut microbiota has been related to the pathophysiology of irritable bowel syndrome. In the human digestive system, bacteria make up the majority of the microorganisms⁸. The order Bacteroidetes, which comprises 90% of the helpful microorganisms in the digestive system, is followed by Firmicutes, Actinobacteria, and Proteobacteria⁹. Individuals of these important phylotypes exhibit a fair

amount of microbial diversity. The host offers the gut microbiota a secure and nutrient-rich habitat, which the host then benefits from in a number of ways. Short-chain fatty acids, vitamin synthesis, energy production, preservation of the intestinal mucosa, and suppression of pathogenic bacteria are all possible under normal physiological conditions. The gut microbiota can also ferment complex, undigested polysaccharide polymers¹⁰. In order to maintain immunological equilibrium, several members of the symbiotic gut microbiota have unique impacts on the host immune system¹¹. A precise balancing act between pro-inflammatory Th17 cells and anti-inflammatory Treg cells in the gut microbiota is necessary to maintain intestinal homeostasis in the host. Segmented filamentous bacteria (SFB) accumulate the pro-inflammatory cytokines Th1 and Th17 in mice¹². Clostridia and Bacteroides bacteria induce T-reg and anti-inflammatory responses. In other studies, it has been demonstrated that antigenic signals from bacteria, such as the retinoic acid produced by Clostridium cluster IV and XIV, the polysaccharide produced by Bacteroides fragilis, and the Faecalibacterium prausnitzii¹³ induce an immune response and a rise in Treg cells. Mice models have demonstrated that the Th17/Treg balance, a crucial element in the emergence and control of colonic inflammation, may be influenced by the gut microbiota.

Mice models of inflammatory bowel disease (IBD) have demonstrated that changes in the gut microbiota lead to intestinal inflammation. Inflammatory lesions in the colon and distal ileum are similar to those seen in humans in most mice models of inflammatory bowel disease. There are more bacteria in the colon and ileum than in the rest of the GIT combined. This lends credence to the hypothesis between gut microbiota and inflammatory lesions¹⁴. Mice models in which the gut microbiota was artificially altered by antibiotic treatment or in which no microorganisms were present (called gnotobiotic mice models) provide functional evidence for the gut microbiota's participation in inflammatory bowel disease.

The results of several studies attempting to anticipate the role of the gut microbiota in intestinal inflammation in inflammatory bowel disease have shown that modification of the gut microbiota is essential to colon inflammation¹⁵. Prebiotics, probiotics, and antibiotics have provided relief for certain IBD patients¹⁶. "Modulation of IBD patients' gut microbiota" cures inflammatory bowel disease by using prebiotics, probiotics, and synbiotics. The exact function that bacteria play in the etiology of illness is still not entirely known, despite the fact that the significance of the intestinal microbiota in intestinal inflammation and IBD pathogenesis has been well documented. It is crucial to comprehend the function of these bacteria with distinctive alterations in the pathogenesis of IBD.

Identified Communities and Species of Bacterial IBD

The aforementioned study supports the notion that the gut microbiota contributes to gut inflammation, however it is still unclear whether a particular bacterial species, strain, or mix of strains is to blame for IBD or just exacerbates it. Numerous studies have found higher frequencies of particular commensal or pathogenic bacterial species/strains in people with IBD, but none of them have been proven to be directly responsible for the onset of the condition. In mice with enteric infections, the ability of one bacterial species to generate chronic

inflammation (colitogenicity) was investigated ¹⁷. *Bacteroides fragilis*-infected mice exhibit persistent intestinal inflammation. The prevalence of *Klebsiella pneumoniae* and *Proteus mirabilis* in the digestive tracts of T-bet-Rag2 mice is linked with the severity of colitis. Adult mice of the Rag2/ and wild-type strains that were exposed to these strains developed colitis. In several human IBD research, adherent/invasive *Escherichia coli* (AIEC), a member of the Enterobacteriaceae family, has been linked to CD. The outcome is granulomatous colitis in boxers. Despite the fact that dysbiosis and the connection of a specific pathogenic, commensal, or opportunistic bacterial species have been demonstrated in IBD patients (figure 1-2) and mouse colitis models (Tables 1), none of these pathogens have been proven to be a cause of IBD according to Koch's postulates. IBD cannot yet be proven to be an infectious illness since Koch's postulates have not been proven to be true. It is still debatable if irritable bowel syndrome is an infectious condition.

Table-1 Mouse models of colitis; there is dysbiosis of the gut microbiota

1.	Increase in <i>Bacteroides distasonis</i> , <i>Akkermansia muciniphila</i> , <i>Clostridium ramosum</i> , and Enterobacteriaceae in dextran sodium sulfate-induced colitis.
2.	Colitis caused by a rise in Enterobacteriaceae and <i>Bacteroides</i> .
3.	<i>Desulfovibrio</i> , and Helicobacteraceae Increased by T-bet/1, Rag2/.
4.	Diversification of gnat-eating mice Reduction in the number of species.

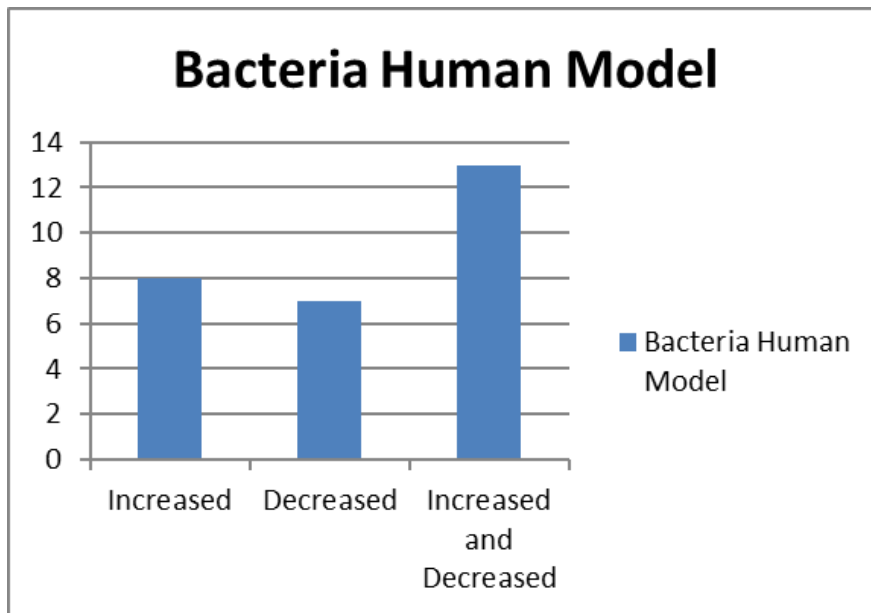


Figure-01

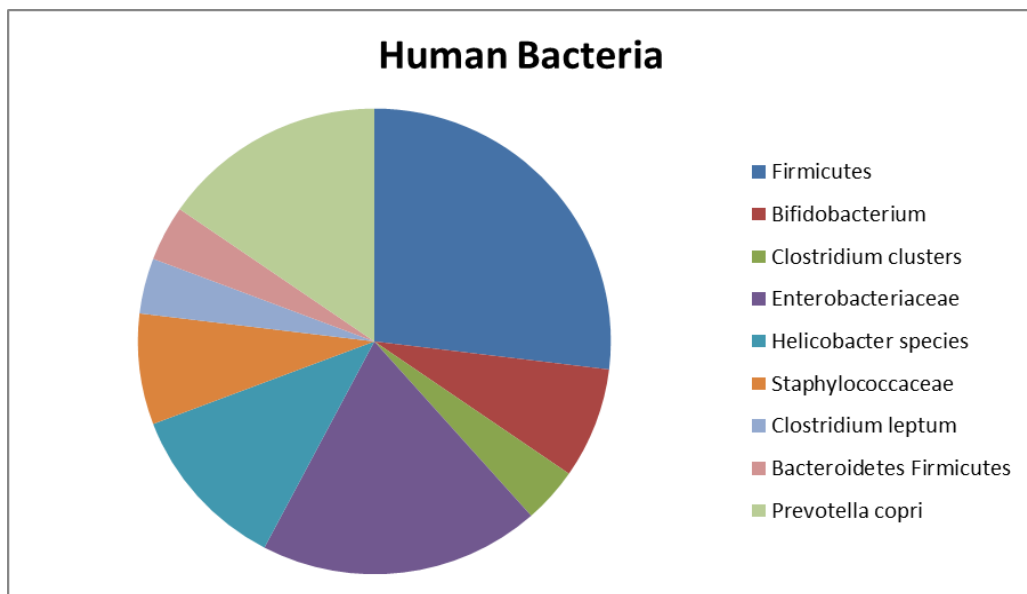


Figure-02

Advancing Knowledge on How to Treat IBD Medicines

Two methods were used in the treatment of the IBD: (1) complementary and (2) alternative medicine, which includes techniques such as spirit concept therapy, fundamental biological therapy, body adjustment therapy, and herbal medicine, may be utilized by patients who have not responded to conventional treatment or who oppose western medicine. CAM is gaining popularity among patients because it is safe, gentle, and effective¹⁸. Herbal medicine and other complementary and alternative medicine (CAM) therapies are gaining popularity for their ability to safely and effectively treat chronic illnesses like IBD. CAM is used to treat IBD in France (21.2%) and Germany (51.3%). Compared to 59.8% of those with UC and 48.3% of those with CD, 47% of the 2,847 Canadians with IBD have tried complementary and alternative medicine (CAM). Herbal medicine (43.6%) and homeopathy (52%) are the two most prevalent CAM therapies. Only 1.6% of Canadians who used CAM reported adverse effects, while the majority of herbal therapy users (41%) reported positive outcomes. Herbal medicine can be used to treat inflammatory bowel disease (IBD) because it regulates the immune system, reduces inflammation, inhibits leukotriene B₄, possesses antioxidant properties, inhibits NF-kappaB, and reduces platelet aggregation¹⁹.

IBD and Herbal treatment

Herbal remedies from traditional Chinese medicine (TCM) have been used for thousands of years to cure and prevent disease²⁰. Due to their low side effects and high efficacy, Chinese HMs manufactured from natural substances are a hot issue in the research and development of new therapies for IBD. Several traditional Chinese medicines, including the Wumei pill decoction, Chaihu peony soup, and Pulsatilla decoction, have been demonstrated to inhibit IBD

development by modifying the composition of gut microbes. However, due to their immunosuppressive and gut microbe-friendly qualities, Chinese HM polysaccharides are ideal prebiotics in IBD adjuvant therapy ²¹, despite being indigestible and not having been proved to restore intestinal flora in IBD patients. Good bacteria like *Lactobacillus* and *Bifidobacteria* are increased, whereas *Enterobacteriaceae* and enterococci are decreased, thanks to the antibacterial effects of astragalus polysaccharide. Polysaccharides from purslane improved intestinal microbiota by increasing *Bifidobacterium* and *Lactobacillus* and decreasing endotoxin in the blood of mice with DSS-induced ulcerative colitis. Polysaccharides from Chinese HM show promise as treatments for immunological diseases because of their ability to modulate Th1 and Th2 cells. The Huangqin-Tang decoction (HQT) improved Th1/Th17 drift and intestinal protective immunity in TNBS-induced colitis by decreasing pro-inflammatory cytokines and their transcription factors and increasing Th2/Treg-associated cytokines ²². Astragalus polysaccharides ameliorated asthma symptoms in a rat model by reducing inflammatory IL-17A and IL-25 while increasing anti-inflammatory IL-35 and IL-10. The cytokines Th17 and Treg were also kept in check. Acid polysaccharides from ginseng reduced IL-1 and IL-17 and increased FOXP3 and Treg cells in animal models of colitis ²².

Synbiotics and Probiotics

Probiotics have shown to be a helpful treatment for a variety of illnesses and conditions, most notably IBD and other gastrointestinal problems, since it was discovered that the gut has a very varied microbiota. Living bacteria known as probiotics are useful. Dairy probiotics can be used to prevent or cure intestinal bacterial overgrowth ²³. Inhibiting pathogenic bacteria, immunological modulation, anti-inflammatory responses, and gut barrier function are how these probiotics operate. Many different types of bacteria, such as *Lactobacillus* species, *Escherichia coli* Nissle 1917 and *Lactococcus lactis*, have been isolated from dairy products. The single probiotic strains *Escherichia coli* Nissle 1917, *Bifidobacteria*, and *Saccharomyces boulardii* are most frequently tried to maintain active UC patients in remission. Probiotics' value has been demonstrated by several DNA investigations ²⁴. Despite the fact that probiotics have been shown to be effective in treating a number of gastrointestinal illnesses, their effects on microbiota repair and health recovery are not fully understood. More research into how probiotics affect gastrointestinal illnesses, particularly inflammatory bowel disease, is thus needed in both laboratory and clinical settings.

Synbiotics have synergistic impacts on host health as opposed to probiotics ²⁵. Combining probiotics and prebiotics is a potential treatment for IBD that may be used in clinical settings and animal models. There is little research supporting the use of symbiotic supplements in IBD. The most typical symbiotic pairings are fructo-oligosaccharides (FOS) and lactobacilli, FOS and lactobacilli, and FOS and lactobacilli. Oligofructose-enriched inulin, *Lactobacillus*, and *Bifidobacterium* were combined to prevent colon cancer and boost IgA and IL-10 production in the colon ²⁶. Compared to a probiotic or prebiotic alone, *Bifidobacterium longum* and psyllium and *B. longum* and inulin-oligofructose both showed a substantial synergistic effect and improved the disease clinical activity index in a randomized controlled research for UC patients ²⁶. Since the advantages of synbiotics vary,

possibly depending on the types and dosages of pre- and probiotics used in various combinations, the scientific community is unable to come to any definite conclusions on the health benefits of synbiotics. Studying synbiotics and their impact on gut inflammatory pathogenic pathways may help treat irritable bowel syndrome (IBS) and other conditions connected to the gut ²⁷. More research on both humans and animals is required in order to provide definitive confirmation and to better understand their immediate health effects, particularly in IBD.

Microbe Transplantation from Fecal

Fecal microbiota transplantation (FMT) is a revolutionary therapy for dysbiosis that employs the use of healthy donor feces. Animal studies have shown that FMT can cure gastrointestinal and metabolic disorders, such as chronic *Clostridium difficile* infection. For chronic *Clostridium difficile* infection, FMT was more effective than medication ²⁸. Of the 16 patients, 13 received FMT (81%), whereas only 4 of the 13 who received antibiotics (31%). The gut microbiota plays a crucial role in inflammatory bowel disease. Possible IBD treatment using FMT. FMT was used to treat UC as early as 1989. For refractory CD, FMT has been shown to be safe, effective, and successful. Moayyedi et al. ³⁰ found that in a randomized study with 70 patients, FMT was safe and resulted in more UC patients remitting than placebo. Colitis did not occur in 13 of 18 UC patients treated with FMT who did not have *C. difficile* infection ²⁹. There were no significant adverse events reported in a phase 1 study of FMT in adolescents with UC. The clinical response rate was 79% after one week.

Conclusion

The incidence of inflammatory bowel disease (IBD) is on the rise across the world. Clinical and chemotherapeutic approaches to IBD that focus on a single possible cause have failed. The microbiome in the gut is the new suspected culprit in inflammatory bowel disease. Multiple studies have linked a dysfunctional microbiome in the stomach to the development of inflammatory bowel disease. Unfortunately, the underlying composition of the gut microbiota and the metabolic indicators that cause IBD are yet unknown. Inflammatory bowel disease (IBD) may be triggered by abnormalities in gut microbiota. Dysfunction of the gut microbiota and metabolic diseases highlight the gut's significance to host physiology. Restoring healthy gut bacteria may help. Gut microbial ecology can be altered and IBD pathogenesis mitigated by using probiotics, prebiotics, synbiotics, or FMT. In this review, we explored the role of gut microbiota targeted treatment methods in IBD therapy, utilizing both animal models and clinical trials, and we summarized the evidence linking the human gut microbiome and intestinal inflammation. In IBD patients, dysbiosis was persistent but not causative. The gut microbiota has a significant effect on illness presentation and activity in mouse models of colitis. Colitis is improved in animal models of inflammatory bowel disease (IBD), however this has not been seen in clinical studies in humans. To learn more about this ecosystem and to pinpoint the core microbiome likely involved in IBD, we need further animal models and clinical research. The optimal bacterial strain or prebiotic for gastrointestinal disorders would likewise be revealed by this environment. Therefore, more research into the causes and treatments of IBD is required.

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