GSC Biological and Pharmaceutical Sciences

eISSN: 2581-3250 CODEN (USA): GBPSC2

Cross Ref DOI: 10.30574/gscbps

Journal homepage: https://gsconlinepress.com/journals/gscbps/

(REVIEW ARTICLE)

Check for updates

Inflammatory bowel disease: A comprehensive review of pathophysiology, clinical presentation and management strategies

Gopal R Sonone *, Pooja R Hatwar, Ravindra L Bakal and Gaurav P Aswar

Shri Swami Samarth Institute of Pharmacy At. Parsodi, Dhamangaon Rly. Dist.-Amravati (444709) Maharashtra, India.

GSC Biological and Pharmaceutical Sciences, 2025, 31(01), 146-155

Publication history: Received on 02 March 2025; revised on 13 April 2025; accepted on 15 April 2025

Article DOI: https://doi.org/10.30574/gscbps.2025.31.1.0152

Abstract

Inflammatory bowel disease (IBD), encompassing Crohn's disease and ulcerative colitis, is a complex and multifactorial disorder characterized by chronic inflammation of the gut mucosa. The exact etiology remains unclear, but it is believed to involve an interplay of genetic, environmental, and immunological factors. The Western diet, rich in fats and sugars, has been implicated in the development of IBD, which affects up to 0.5% of the general population in Western countries. The gut microbiome plays a crucial role in IBD pathophysiology, with dysbiosis contributing to inflammation and disease progression. Clinical presentation varies, with symptoms ranging from gastrointestinal issues to extraintestinal manifestations. Diagnosis involves a combination of clinical symptoms, serology, imaging, and endoscopic appearance. Management strategies include exclusive enteral feeding, immunomodulators, aminosalicylates, and corticosteroids. Medication adherence is essential to improve clinical outcomes and reduce the risk of complications. This review aims to summarize the current understanding of IBD pathophysiology, clinical presentation, and management strategies, highlighting the complexities of this multifaceted disease.

Keywords: Inflammatory bowel disease; Crohn's disease; Ulcerative colitis; Gut microbiome; Dysbiosis

1. Introduction

Chronic inflammation of the gut mucosa is a hallmark of inflammatory bowel diseases (IBD), which include ulcerative colitis (UC), Crohn's disease (CD), and unclassified inflammatory bowel disease (IBD-U) [1]. Although the clinical course of IBD is unpredictable, it typically consists of remission intervals punctuated by acute or sub acute exacerbations, or "flares," for which there are several reasons. Extra intestinal symptoms may manifest independently of luminal symptoms or in conjunction with gastrointestinal (GI) symptoms [2]. It is still unclear how precisely these elements interact. Believed that the Western diet, which is heavy in fats and sugars and low in fruits and vegetables, plays a role in the development of IBD because it is the most common in the Western world, where it affected up to 0.5% of the general population in 2015. It is known that the condition finally renders the Western diet ineffective decreases the gut microbiome's diversity between 5 and 15 [3]. According to the group, 80% of CD patients will require at least one operation in their lifetime, and 32.9% of UC patients needed a colectomy. These findings have a significant impact on quality of life. Strict and efficient management of IBD patients is essential to improving their prognosis [4]. Based on 58 studies with 18,915 patients, the combined prevalence of anxiety symptoms in IBD patients was 32.1% (95% CI 28.3% to 36.0%; I2=96.9%, p<0.001). Two Spanish studies (716 and 793 patients, respectively) had the lowest pooled prevalence of anxiety symptoms among IBD patients (10.5%), while two Iranian studies (108 and 120 patients, respectively) had the highest pooled prevalence (56.2%) [5]. The first three epidemiological stages of IBD progression are presently present in every part of the world, and all four stages will eventually be reached. Developing nations are presently in the first stage of evolution, known as "emergence," and if their economies grow and their society become more westernized, they should anticipate moving into the second stage. The second stage (Acceleration in Incidence) is where the majority of recently industrialized nations are currently located, but if these areas adopt Western

* Corresponding author: Gopal R Sonone

epidemiological trends, they are probably going to move into the third stage within the course of the next three decades [6].

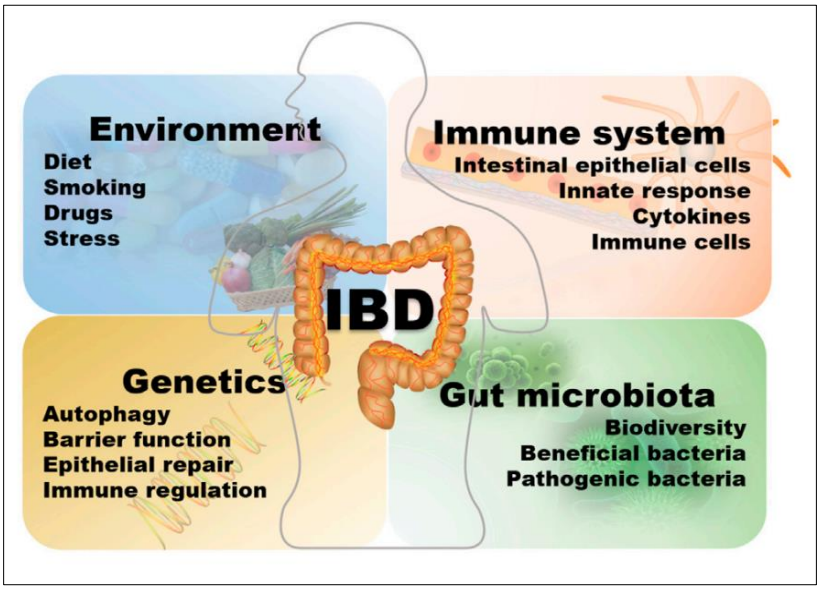

Figure 1 The etiology of IBD [7]

Although incidence rates seem to have stabilized with high burden and prevalence, IBD has historically been thought of as a disease that only affects industrialized and wealthy countries. In newly industrialized nations, the prevalence of IBD is currently quickly increasing (GBD 2017 Inflammatory Bowel Disease Collaborators, 2020) [8]. Chronic recurrent inflammation of the gastrointestinal system with acute flare-ups and remission periods is the hallmark of IBD. Diarrhea, persistent stomach pain, and extraintestinal symptoms such arthritis, mouth ulcers, and skin lesions are common clinical characteristics of CD and UC patients. Regarding issues related to the eyes Nonetheless, there are some distinctions between the two IBD clinical presentations. In the prognosis, inflammatory load, and underlying pathophysiology UC is distinguished by the participation of the CD patients exhibit patchy lesions throughout the colon, primarily in the mucosal layer. Gastrointestinal system, which includes the mouth and the anus, is marked by fistulae, transmural inflammation, Intestinal blockages and abdominal abscesses [9]. Human and rodent intestinal mucosa are colonized by the Gram-negative, anaerobic bacterium Akkermansia muciniphila, which breaks down mucus layers. There is an inverse relationship between the abundance of A and meta-genomic data. Muciniphila and illnesses such diabetes, obesity, and inflammatory bowel disease (IBD). Consequently, in recent years, this bacterium's promise as an immune-modulatory probiotic for autoimmune diseases including Experimental models of chronic inflammatory disorders have been investigated. According to reports, A. muciniphila slows down the onset and progression of diabetes, obesity, and IBD in mice, which is consistent with these human association studies. Clinical research involving patients who are obese or have diabetes is therefore being carried out, and the initial findings are really encouraging. Consequently, this brief analysis emphasizes the primary conclusions on the advantageous functions of A muciniphila and its modes of action in Chronic inflammatory and autoimmune disorders [10]. Their quality of life has significantly changed over time, accompanied by crippling morbidity and exacerbations, according to historical statistics. Although the exact cause of IBD is unknown, current theories suggest that environmental and immunological regulatory factors interact. Characteristics of those who are genetically susceptible younger people are more prone to IBD, which can lead to a substantial change in their quality of life, as well as exacerbations and crippling morbidity. The Although the exact cause of IBD is unknown, current theories suggest a combination of Immunological and environmental regulatory variables in people who are genetically susceptible [11].

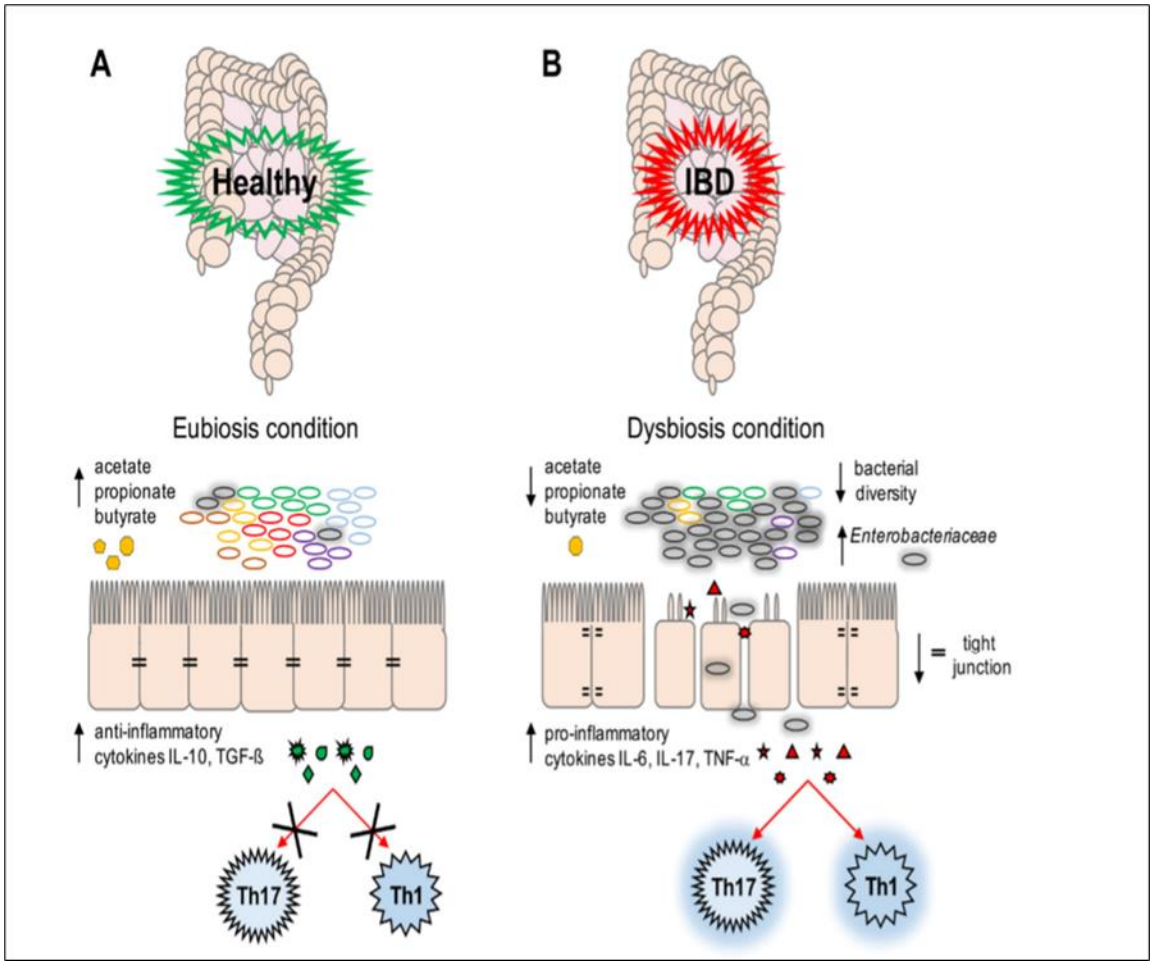

Figure 2 An illustration of the situations of dysbiosis (B) and eubiosis (A). (A) By: (i) generating short-chain fatty acids (SCFAs), such as acetate, propionate, and butyrate; (ii) inhibiting the growth of any microbial pathogens; and (iii), microbiota contributes significantly to the preservation of gut stability. regulating the immune system, such as by generating cytokines that reduce inflammation (Interleukin (IL)-10, Reducing T-helper cell (Th)17 and Th1 activation and transforming growth factor (TGF)-β) cells; (B) Under dysbiotic circumstances, Enterobacteriaceae family bacteria could overgrow, which reduces gut integrity and bacterial diversity. This is demonstrated by a decline in in the synthesis of SCFA, and concurrent rises in pro-inflammatory cytokines such IL-6, IL-17, and tumour TNF-α, a necrosis factor that activates the inflammatory response is mediated by Th1 and Th17 cells. Additionally, there is a reduction in tight junctions, which leads to a loss of intestinal epithelial impermeability [12]

2. Pathophysiology of Inflammatory Bowel Disease:

The central nervous system (CNS), which plays a major role in autonomic pathways, the enteric nervous system, the hypothalamic-pituitary-adrenal (HPA) axis, and serotonin signaling are some examples of the neuro-hormonal elements engaged in bidirectional communication. Additionally, changed in-testinal Barriers, the intestinal immune response, and the makeup and activity of the gut microbiota may all play a role to changed gut-brain communication. Additionally, the gut microbiome may be a source of neurotransmitters. such as gamma-aminobutyric acid (GABA) and serotonin, which are involved in mood and stomach regulation. In individuals with IBD, changes in the host-gut microbiome interaction, including neurotransmitter activity, may lead to GI symptoms as well as anxiety and depression [13]. By demonstrating that defects in several biological systems contribute to the pathophysiology of IBD, genetic study has shed significant light on the disease's etiology IBD pathophysiology is a complex illness. Both environmental and genetic variables play a role in the pathophysiology of IBD. Participate Germline-derived nucleotide sequence has been the subject of earlier studies of genetic variables in IBD. Variations and somatic mosaic changes, which could impact the course of the disease, its onset, or both, have Been documented in IBD patients [14]. Genetic elements. GWAS (genome-wide association studies), following More than 240 non-overlapping genetic risk factors have been found through generation sequencing research and other analysis. Loci, of which Crohn's disease and ulcerative colitis share about 30 genetic loci. The examination of the genes and genetic loci linked to IBD shows that several processes, including innate

mucosal defence, epithelial barrier function, digestive homeostasis, Autophagy, cell migration, adaptive immunity, immunological control, and metabolic processes related to with the homeostasis of cells [15]. The collection of bacteria and their genes present in their host organ is known as the microbiome, and it has become crucial to our comprehension of both health and illness. One of the main characteristics of IBD is dysbiosis, which is an imbalance in the gut microbiome's composition. This is distinguished by the loss of Diversity of microbes, especially those that produce short-chain fatty acids (SCFAs) and are anaerobic Bacteria, including Faecal bacterium prausnitzii, and a rise in unfavorable adherents in addition to invasive pathogens like adherent-invasive Escherichia coli. Our comprehension of the Function of the microbiome is derived from the study of the gathering of metabolites resulting from the gut microbiota's activity and function; and is still Deepen [16]. Along with other lifestyle modifications, western diets heavy in simple carbs and saturated fats and deficient in dietary fiber have been implicated in contributing to the sharp increase in ibd diagnoses in recently industrialized nations. One major and significant factor in the formation of gut microbes is diet. And purpose According to one study in animals, a diet low in fiber for several generations causes Gradual and permanent alterations in the gut microbiota, such as a decline in diversity and the loss of Microbes that degrade polysaccharides A meta-analysis of IBD observational research has linked Risk factors include urban life, smoking, not nursing, pollution, and exposure to xenobiotic In addition to the diet. Circadian disturbances have been linked in a number of studies to increased intestinal inflammation and more severe CD [17]. Any disruption or dysregulation of the gut microbiota can lead to disease states because it is a crucial physical, chemical, and immunological interaction between the host and environment. For example, a reduced mucus layer, altered responses to physical epithelial barrier function, and Mutations in MUC19, ITLN1, FUT2, and XBP1 have all been linked to endoplasmic reticulum stress. as IBD risk factors at the moment, it is thought that the pathophysiology of human IBD includes inappropriate immune system activation upon exposure to gastrointestinal antigens in genetically vulnerable people, like elements of the microbiome [18]. Although the exact cause of PSC-IBD is still unknown, new research indicates that a number of factors, such as genetic predisposition, the immune-mediated route, changes in bas, and gut dysbiosis, may be involved. Furthermore, the PSC-IBD patients clinical characteristics differ significantly from those of IBD-only patients, indicating that PSC-IBD is a distinct medical condition. Additionally, the strong correlation between PSC and IBD probably indicates a significant illustration of how clinical illness can result from disruption of the gut-liver axis [19].

3. Types of Inflammatory Bowel Disease

3.1. Crohn's Disease

Crohn's disease is a chronic inflammatory disease of the gastrointestinal tract that is becoming more and more common worldwide. It may be caused by a complex interaction between genetic susceptibility, environmental factors, and altered gut microbiota, which results in dysregulated innate and adaptive immune responses. Inflammatory bowel disease (IBD) is a long-standing, relapsing inflammatory disease that affects different parts of the gastrointestinal tract and includes Ulcerative Colitis [20]. Crohn's disease is thought to be caused by a combination of genetic susceptibility, environmental factors, and intestinal microbiota, which leads to an aberrant mucosal immune response and impaired epithelial barrier function [21].

3.2. Ulcerative Colitis

Colonic mucosal inflammation and a chronic relapsing course are the hallmarks of ulcerative colitis, an idiopathic inflammatory bowel disease that is typically mildly active but can be fatal during severe attacks due to colonic and systemic complications and later in the course of the disease due to the development of colorectal cancer. It is estimated that 15% of patients with ulcerative colitis experience an acute attack of severe colitis, and 30% of these patients need a colectomy [22]. When rectal bleeding stops and the frequency of bowel movements returns to normal, this is referred to as clinical remission. In clinical studies, complete remission is used to show safety and efficacy. It is characterized by normal stool frequency, no rectal bleeding, and a normal or quiescent mucosal look at sigmoidoscopy. Registration remission: now employed by regulatory bodies, used in drug license trials; Demands that rectal bleeding stop and that the Mayo Clinic sigmoidoscopy score be either 0 or 1. The normal appearance of the rectal mucosa or erythema alone is the Ulcerative Colitis Disease Activity Index [23].

3.3. Indeterminate Colitis

When a surgical specimen from a patient having a colectomy for inflammatory bowel disease (IBD) did not have a histological image typical of Crohn's disease (CD) or ulcerative colitis (UC), the term "indeterminate colitis" (IC) was first used in 1978. Numerous investigations have It has been repeatedly demonstrated that in 5% to 15% of cases, such a diagnosis might be made. But as much as two-thirds when all clinical symptoms are present, some of these people may eventually be categorized as having one of the two main types of IBD. Endoscopic and radiological evidence were

considered [24]. Because of an aggression that causes tissue damage, colitis is characterized by changes to the mucosa and subsequently the deeper layers. In endoscopic biopsies, three readily identifiable histological types are used for the mucosa. Characteristics that have been found and statistically confirmed to have the capacity to precisely identify Colitis [25]. Before creating a definitive categorization, indeterminate colitis (IC) was suggested as a temporary Final diagnosis of either UC or CD, and it is a subset of IBD that involves inflammation of the mucosa. With difficult-to-distinguish clinical and pathological characteristics [26]. May be There are no known prospective medical therapy trials for indeterminate colitis. In one retrospective investigation, twenty patients with indeterminate colitis that was extremely active and medically refractory were given one to sixteen infliximab infusions. Infliximab was effective for 16 out of 20 patients, and eight of the After some time, 16 responders were classed as having crohn's disease. Interestingly, there was a comparable Response over time between the eight individuals who were still diagnosed with indeterminate colitis and those who Crohn's disease. Additional research on the use of 6-thioguanine with infliximab tacrolimus18 has included Patients with ulcerative and indeterminate colitis, making it challenging to assess the effectiveness of the Group with uncertain colitis. Until there is a widely recognized positive diagnostic test to use as an inclusion criterion, it is unlikely that patients with indeterminate colitis will participate in a prospective randomized medical treatment trial [27].

4. Clinical Representation

4.1. Symptoms and Sign

Idiopathic diseases of the gastrointestinal tract include Crohn's disease, ulcerative colitis, and inflammatory bowel disease. These three conditions are typically grouped together due to commonalities, such as gastrointestinal inflammation, symptoms that wax and wane in severity, and unknown cause. However, they exhibit distinct symptoms, microscopic features, and gastrointestinal tract patterns [28]. 771 patients who provided HADS-anxiety data at baseline and two or more follow-up points, those whose HADS-anxiety scores were either continuously abnormal or worsening (105 (13.6%) patients) or fluctuating (266 (34.5%) patients) were substantially More likely to be female ($p<0.001$) and younger ($p<0.001$) than those who have consistently 400 individuals (51.9%) had scores that were normal or improving [29]. Carried out a retrospective analysis with the goal of elucidate the clinical features, therapeutic trends, and demographics of IBD patients aged 60 Years of age or older. Every patient who has an IBD diagnosis and is being followed up with at King Abdul-Aziz KAUH (University Hospital) [30].

4.2. Extraintestinal manifestation

Extra intestinal manifestations (EIMs) are thought to affect about 27% of individuals with UC, with a quarter of EIMs occurring before the diagnosis of UC, according to a meta-analysis of 14 studies (N = 8925 UC patients). Box 1 lists the EIMs of UC, stratified by those that are exacerbated vs. independent of bowel inflammation, as well as comorbidities associated with UC. When gastrointestinal symptoms are present at the same time, the presence of an EI moran associated comorbidity should raise clinical suspicion of an underlying diagnosis of IBD [31]. A sizable fraction of IBD patients are not responsive to traditional medication treatment. Annual recurrence rates can reach 25–40% even with appropriate dosages of 5-aminosalicylic acids (5-ASA) and/or azathioprine. Probiotics and prebiotics: an introduction. Into the diet can aid in the restoration of the natural vegetation and stop the spread of harmful germs by creating antimicrobial peptides and enhance gut health by promoting the development and function of beneficial bacteria by fermentation that is prebiotic [32]. Even while IBD's extra intestinal symptoms might affect the skin, eyes, and joints, up to 50% of cases can also involve the mouth. Up to 80% of children with IBD may have oral symptoms, frequently in the gingiva, with a higher frequency in CD and men. Despite conflicting reports, it has been estimated that up to 25% of IBD cases have oral, the most commonly reported mouth symptoms prior to any intestinal involvement symptoms include ulceration of the oral mucosa and the development of "cobble stoning," in addition to Persistent, severe gingival/period ontium inflammation [33].

4.3. Diagnosis

Using proteomics, a cross-sectional study that assessed 40 CD patients 20 of them, or 50% of the patients, had stricturing disease discovered hepatocyte growth factor activator (HGFA) and cartilage oligomeric matrix protein (COMP). Greater in stricture patients than in those with an inflammatory phenotype. This marker Profile might be useful in the future following a comprehensive validation campaign, considering its pathophysiologic Significance in fibrogenesis and, hence, a potential direct connection to the disease's fibrotic burden [34]. Even though these distinctive diagnostic results are well recognized, none of the individual items are specifically tailored for IBD. Therefore, a combination of clinical symptoms, serology, imaging and endoscopic appearance, and histopathology is always used to make a diagnosis. The differential diagnosis encompasses a wide range of range of inflammatory conditions that might exacerbate pre-existing IBD or that resemble it. [35].

- If UC is suspected based on clinical signs, a colonoscopy is required to confirm the diagnosis.

- A colonoscopy is done to assess the severity of the disease and confirm the diagnosis of UC [36].

4.4. Management of Inflammatory Bowel Disease

There is a substantial and established body of evidence supporting the effectiveness of exclusive enteral feeding in causing (and sustaining) Crohn's disease. Up to 80% of pediatric patients with Crohn's disease can experience remission because to it; nonetheless, the emphasis is on expanding dietary choices and IBD, both in terms of etiology and therapy. Partial enteral nutrition and new diets even if nutrition and dietary management are popular, there is substantial evidence that no "normal" food diet may effectively induce remission in IBD, including Fermentable oligosaccharides (FODMAPs) include monosaccharides, polyols, disaccharides, and charides Vegetarian, Terranean, and other exclusionary diets (such dairy or wheat) [37].

4.5. Diet, Lifestyle, and Environmental Factors

Circadian disturbances have been linked in a number of studies to increased intestinal inflammation and more severe CD. Additionally, some gut microbiota members may be disrupted by diurnal oscillations, which could lead to host-microbe interaction imbalances and increase the risk and progression of IBD [38]. In addition to avoiding complex carbs and disaccharides, the Specific carbs diet (SCD) calls for avoiding wheat grains, oats, barley, corn, quinoa, rice, and dairy products (apart from hard cheeses and lacto-fermented goods). And the use of honey in place of sugar [39]. The bacteria that live in the distal gut and are essential to its management use dietary fiber as a substrate. About 17 enzymes are produced by humans to break down fiber. But in order to depolymerize and ferment, these bacteria generate thousands of complimentary enzymes. Dietary polysaccharides into SCFAs that the host can absorb [40].

4.6. Medical Therapy

There are a variety of medical therapies available to treat both UC and CD, including 5-aminosalicylic acid (5-ASA) drugs, cortico-steroids, immunosuppressive agents, biological therapies, and anti-biotics. These Agents can heal active disease, prevent relapse, and improve the quality of life but the relative efficacy of these competing therapies is unclear [41].

4.7. Immunomodulators

Azathioprine (AZA) and 6-mercaptopu-rine (6MP) are two immunomodulators that have long been used to treat UC and CD. However, it takes two to four months for these medications to take full impact. As a result, these medications are typically used in conjunction with another type of treatment until their levels stabilize. To avoid colectomy, cyclosporine has been given in cases with severe colitis that are steroid-refractory [42]. Cytokine release was deemed modulated by ISG15 only when the concentration of cytokines in the conditioned medium surpassed 1000 pg/ml in comparison to the untreated control, as determined through multiplex experimentation. [43].

4.8. Aminosalicylate

For more than 40 years, sulfasalazine has been the parent amino salicylate in use. Many oral and rectal 5-ASA formulations have been developed because of the realization that the 5-aminosalicylic acid [5-ASA, mesalazine (mesalamine)] Component is the active moiety in ulcerative colitis. Olsalazine, a 5-ASA dimer, sulfasalazine (sulfapyridine coupled to 5-ASA), and, most recently, balsalazide (5-ASA linked to 4-aminobenzoyl-b-alanine, an inert carrier) are examples of seven 5-ASA conjugates. Oral mesalazine formulations include a prolonged-release formulation (Pentasa) and ph-released formulations (Asacol, Salofalk, and Claversal) [44]. Clinical efficacy of amino salicylates in IBD The way amino salicylates are delivered may have a clinical impact. However, a dose-related toxicity that restricts SASP's dose-response 30% of patients clinical utility The goal of more recent 5-ASA formulations is to preserve SASP's therapeutic benefits while avoiding its negative side effects [45].

4.9. Cortico-Steroids

Not surprisingly, given the documented toxicity of long-term corticosteroid usage, key bodies have created quality indicators and standards with the express goal of reducing patient exposure to corticosteroids. The revised 2017 consensus guidelines from the European Crohn's and Colitis Organization (ECCO) On UC diagnosis and treatment highlight that the key objective of maintenance SS Therapy is to sustain remission without the use of steroids. According to the Crohn's and Colitis Foundation of America (CCFA), The proportion of patients on prednisone (not include those who received a diagnosis within the prior 112 days) As an IBD unit's quality outcome measure [46]. Adequate Use of Corticosteroids should not be used to maintain remission in IBD because they have no demonstrated effectiveness in this regard. Clinically significant adverse effects include hyperglycemia in people with Diabetes that coexists. As a result, continued use increases the chance of serious side effects. Patients who are refractory should be evaluated for alternate

therapies. To corticosteroids, which are described as Necessitating ongoing use for more than three months or a repeat course within three months) [47].

4.10. Medication Adherence

The medication adherence report Scale (MARS), which gauges a variety of adherence behaviors, was used to evaluate medication adherence. In this context, non-adherence is operationalized by the propensity to change the dosage from prescribed medications or to avoid, forget, or stop taking them altogether. That the doctor has advised [48]. Improving IBD patients' medication compliance may Enhance clinical results and lower the long-term risk of CRC development. A positive doctor-patient relationship has been linked to higher drug adherence rates, and communication is essential to enhancing patient adherence [49].

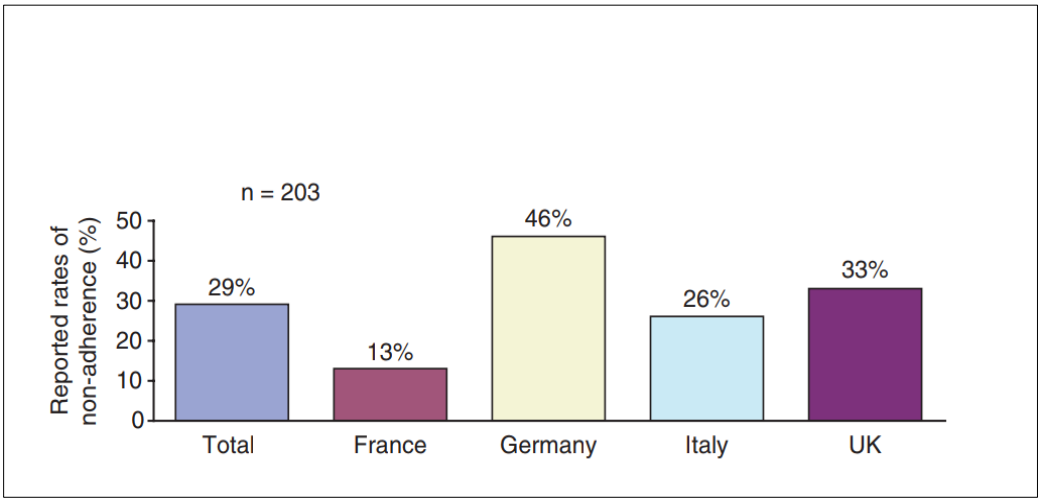

Figure 3 Self-reported medication non-adherence rates vary by culture [49].

5. Treatment Related Adverse Effects

5.1. Hypersensitivity reactions

Acute infusion reactions and delayed hypersensitivity are just two examples of the many ways that hypersensitivity reactions manifest. Anaphylaxis is a symptom of type I acute hypersensitivity reactions, which are IgE mediated. Type II are complement-mediated and cytotoxic Type III is associated with the immunological complex and manifests as serum sickness. T lymphocytes mediate type IV cell-mediated delayed hypersensitivity [50]. Numerous medications, such as amino salicylates, corticosteroids, antibiotics, immunological suppressors, and biological agents (anti-TNF [tumor necrosis factor]), are used in the medical treatment of Crohn's disease (CD) and ulcerative colitis (UC). Every type of drug has a place in the treatment of various illnesses, and the primary goal of patient care is to increase therapeutic effectiveness while lowering toxicity [51]. Due to the less aggressive course of the disease in patients with an elderly beginning, the care of IBD in these patients may deviate from normal practice for adult patients [52].

6. Conclusion

Inflammatory Bowel Disease (IBD) is a complex and multifactorial disease requiring a comprehensive understanding of its pathophysiology, clinical presentation, and management strategies. The gut microbiome plays a crucial role in IBD development and progression, and dysbiosis is a key contributor to inflammation and disease severity. While current management strategies, including exclusive enteral feeding and immunomodulators, have shown efficacy, there is a need for further research to develop more effective and targeted therapies. Improving medication adherence and addressing extraintestinal manifestations are also essential to enhance clinical outcomes and quality of life for IBD patients. By the complexities of IBD, we can develop more effective management strategies and improve patient care. Further studies are necessary to explore the interplay between genetic, environmental, and immunological factors in IBD development and progression, ultimately leading to better patient outcomes.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] Akutko, Katarzyna, and Andrzej Stawarski. "Probiotics, Prebiotics and Synbiotics in Inflammatory Bowel Diseases." Journal of clinical medicine 2021; 10(11): 1-13,

[2] Rustgi SD, Kayal M, Shah SC. Sex-based differences in inflammatory bowel diseases: a review. Therap Adv Gastroenterol. 2020; 28(13):1-10

[3] Campmans-Kuijpers MJE, Dijkstra G. Food and Food Groups in Inflammatory Bowel Disease (IBD): The Design of the Groningen Anti-Inflammatory Diet (GrAID). Nutrients. 2021;13(4):1-34.

[4] Chen P, Zhou G, Lin J, Li L, Zeng Z, Chen M, Zhang S. Serum biomarkers for inflammatory bowel disease. Frontiers in Medicine. 2020; 22(7):1-25.

[5] Barberio B, Zamani M, Black CJ, Savarino EV, Ford AC. Prevalence of symptoms of anxiety and depression in patients with inflammatory bowel disease: a systematic review and meta-analysis. The Lancet Gastroenterology & Hepatology. 2021; 16(5):359-370.

[6] Kaplan GG, Windsor JW. The four epidemiological stages in the global evolution of inflammatory bowel disease. Nature reviews Gastroenterology & hepatology. 2021; 18(1):56-66.

[7] Duan L, Cheng S, Li L, Liu Y, Wang D, Liu G. Natural Anti-Inflammatory Compounds as Drug Candidates for Inflammatory Bowel Disease. Front Pharmacol. 2021; 14(12):1-22

[8] Luzentales-Simpson M, Pang YCF, Zhang A, Sousa JA, Sly LM. Vedolizumab: Potential Mechanisms of Action for Reducing Pathological Inflammation in Inflammatory Bowel Diseases. Front Cell Dev Biol. 2021; 3(9):1-10

[9] Saez A, Gomez-Bris R, Herrero-Fernandez B, Mingorance C, Rius C, Gonzalez-Granado JM. Innate lymphoid cells in intestinal homeostasis and inflammatory bowel disease. International journal of molecular sciences. 2021; 22(14):1-24.

[10] Rodrigues VF, Elias-Oliveira J, Pereira ÍS, Pereira JA, Barbosa SC, Machado MS, Carlos D. Akkermansia muciniphila and gut immune system: a good friendship that attenuates inflammatory bowel disease, obesity, and diabetes. Frontiers in immunology. 2022; 7(13): 1-8

[11] Mosli M, Alawadhi S, Hasan F, Abou Rached A, Sanai F, Danese S. Incidence, prevalence, and clinical epidemiology of inflammatory bowel disease in the Arab world: A systematic review and meta-analysis. Inflammatory Intestinal Diseases. 2021; 76(3):123-131.

[12] Baldelli V, Scaldaferri F, Putignani L, Del Chierico F. The role of Enterobacteriaceae in gut microbiota dysbiosis in inflammatory bowel diseases. Microorganisms. 2021; 9(4):1-15.

[13] Aliu A, Bosch DH, Keszthelyi D, Rezazadeh Ardabili A, Colombel JF, Sawyer R, Törnblom H, Hart A, Jonkers DM, Pierik MJ, Mujagic Z. A practical approach to persistent gastrointestinal symptoms in inflammatory bowel disease in remission. Alimentary Pharmacology & Therapeutics. 2024;59(12):1470-1488.

[14] Kakuta Y, Naito T, Kinouchi Y, Masamune A. Current status and future prospects of inflammatory bowel disease genetics. Digestion. 2023; 104(1):7-15.

[15] Guan Q. A comprehensive review and update on the pathogenesis of inflammatory bowel disease. Journal of immunology research. 2019;(1):1-16.

[16] Wark G, Samocha-Bonet D, Ghaly S, Danta M. The role of diet in the pathogenesis and management of inflammatory bowel disease: a review. Nutrients. 2020; 13(1):1-15

[17] Qiu P, Ishimoto T, Fu L, Zhang J, Zhang Z, Liu Y. The gut microbiota in inflammatory bowel disease. Frontiers in cellular and infection microbiology. 2022; 22(12):1-21

[18] Santana PT, Rosas SL, Ribeiro BE, Marinho Y, de Souza HS. Dysbiosis in inflammatory bowel disease: pathogenic role and potential therapeutic targets. International journal of molecular sciences. 2022; 23(7):1-25.

[19] Kim YS, Hurley EH, Park Y, Ko S. Primary sclerosing cholangitis (PSC) and inflammatory bowel disease (IBD): a condition exemplifying the crosstalk of the gut–liver axis. Experimental & molecular medicine. 2023; 55(7):1380-1387.

[20] Younis N, Zarif R, Mahfouz R. Inflammatory bowel disease: between genetics and microbiota. Mol Biol Rep. 2020; 47(4):3053-3063.

[21] Torres J, Mehandru S, Colombel JF, Peyrin-Biroulet L. Crohn's disease. The Lancet. 2017; 389(10080):1741-1755.

[22] Caprilli R, Viscido A, Latella G. Current management of severe ulcerative colitis. Nature Clinical Practice Gastroenterology & Hepatology. 2007; 4(2):92-101.

[23] Travis SP, Higgins PD, Orchard T, Van Der Woude CJ, Panaccione R, Bitton A, O'Morain C, Panes J, Sturm A, Reinisch W, Kamm MA. Defining remission in ulcerative colitis. Alimentary pharmacology & therapeutics. 2011; 34(2):113-124.

[24] Meucci G. What is the incidence, prevalence, and natural history of indeterminate colitis?. Inflammatory bowel diseases. 2008; 1 (14):159-160.

[25] Geboes K, Van Eyken P. Inflammatory bowel disease unclassified and indeterminate colitis: the role of the pathologist. J Clin Pathol. 2009;62(3):201-205

[26] Venkateswaran N, Weismiller S, Clarke K. Indeterminate Colitis – Update on Treatment Options. J Inflamm Res. 2021; 30(14):6383-6395.

[27] Tremaine WJ. Indeterminate colitis–definition, diagnosis and management. Alimentary pharmacology & therapeutics. 2007;25(1):13-17.

[28] Norouzkhani N, Faramarzi M, Ghodousi Moghadam S, Karimi MA, Shokri Shirvani J, Bahari A, ShojaeiBaghini M, Eslami S, Tabesh H. Identification of the informational and supportive needs of patients diagnosed with inflammatory bowel disease: a scoping review. Frontiers in Psychology. 2023; 11(14):1-17

[29] Fairbrass KM, Guthrie EA, Black CJ, Selinger CP, Gracie DJ, Ford AC. Characteristics and effect of anxiety and depression trajectories in inflammatory bowel disease. Official journal of the American College of Gastroenterology ACG. 2023; 118(2):304-316.

[30] Mosli MH, Alghamdi MK, Bokhary OA, Alzahrani MA, Takieddin SZ, Galai TA, Alsahafi MA, Saadah OI. Inflammatory bowel disease in the elderly: A focus on disease characteristics and treatment patterns. Saudi Journal of Gastroenterology. 2023 ;29(4):212-219.

[31] Gros B, Kaplan GG. Ulcerative colitis in adults: a review. Jama. 2023; 330(10):951-965.

[32] Guo X, Huang C, Xu J, Xu H, Liu L, Zhao H, Wang J, Huang W, Peng W, Chen Y, Nie Y. Gut microbiota is a potential biomarker in inflammatory bowel disease. Frontiers in Nutrition. 2022; 21(8):1-11

[33] Byrd KM, Gulati AS. The "gum–gut" axis in inflammatory bowel diseases: A hypothesis-driven review of associations and advances. Frontiers in immunology. 2021; 19(12):1-18

[34] Steiner CA, Berinstein JA, Louissaint J, Higgins PD, Spence JR, Shannon C, Lu C, Stidham RW, Fletcher JG, Bruining DH, Feagan BG. Biomarkers for the prediction and diagnosis of fibrostenosing Crohn's disease: a systematic review. Clinical Gastroenterology and Hepatology. 2022; 20(4):817-846.

[35] Gecse KB, Vermeire S. Differential diagnosis of inflammatory bowel disease: imitations and complications. The lancet Gastroenterology & hepatology. 2018; 3(9):644-653.

[36] Nakase H, Uchino M, Shinzaki S, Matsuura M, Matsuoka K, Kobayashi T, Saruta M, Hirai F, Hata K, Hiraoka S, Esaki M. Evidence-based clinical practice guidelines for inflammatory bowel disease 2020. Journal of gastroenterology. 2021 ;56(6):489-526.

[37] Ashton JJ, Beattie RM. Inflammatory bowel disease: recent developments. Archives of disease in childhood. 2024 ;109(5):370-376.

[38] Shan Y, Lee M, Chang EB. The gut microbiome and inflammatory bowel diseases. Annual review of medicine. 2022 ;73(1):455-468.

[39] Godala M, Gaszyńska E, Zatorski H, Małecka-Wojciesko E. Dietary interventions in inflammatory bowel disease. Nutrients. 2022; 14(20):1-21

[40] Baumgart DC, Le Berre C. Newer biologic and small-molecule therapies for inflammatory bowel disease. New England Journal of Medicine. 2021; 385(14):1302-1315.

[41] Talley NJ, Abreu MT, Achkar JP, Bernstein CN, Dubinsky MC, Hanauer SB, Kane SV, Sandborn WJ, Ullman TA, Moayyedi P, American College of Gastroenterology IBD Task Force. An evidence-based systematic review on medical therapies for inflammatory bowel disease. Official journal of the American College of Gastroenterology| ACG. 2011; 1(106):2-25.

[42] Harris A, Feller ER, Shah SA. Medical therapy of IBD in 2009. Medicine and Health Rhode Island. 2009; 92(3):78-81

[43] Eiden KA. Nutritional considerations in inflammatory bowel disease. Practical Gastroenterology. 2003; 27 (5):33-54.

[44] Hanauer SB. Aminosalicylates in inflammatory bowel disease. Alimentary pharmacology & therapeutics. 2004; 20:60-65.

[45] Campregher C, Gasche C. Aminosalicylates. Best practice & research Clinical gastroenterology. 2011; (4-5):535-546.

[46] Dorrington AM, Selinger CP, Parkes GC, Smith M, Pollok RC, Raine T. The historical role and contemporary use of corticosteroids in inflammatory bowel disease. Journal of Crohn's and Colitis. 2020; 14(9):1316-1329.

[47] Barrett K, Saxena S, Pollok R. Using corticosteroids appropriately in inflammatory bowel disease: a guide for primary care. British Journal of General Practice. 2018; 68(675):497-498.

[48] Ediger JP, Walker JR, Graff L, Lix L, Clara I, Rawsthorne P, Rogala L, Miller N, McPhail C, Deering K, Bernstein CN. Predictors of medication adherence in inflammatory bowel disease. Official journal of the American College of Gastroenterology ACG. 2007 ;102(7):1417-1426.

[49] Robinson A. Improving adherence to medication in patients with inflammatory bowel disease. Alimentary Pharmacology & Therapeutics. 2008; (27):9-14.

[50] Shivaji UN, Sharratt CL, Thomas T, Smith SC, Iacucci M, Moran GW, Ghosh S, Bhala N. managing the adverse events caused by anti-TNF therapy in inflammatory bowel disease. Alimentary pharmacology & therapeutics. 2019; 49(6):664-680.

[51] Scribano ML. Adverse events of IBD therapies. Inflammatory bowel diseases. 2008;15(14):1438-1447.

[52] Calafat M, Mañosa M, Cañete F, Ricart E, Iglesias E, Calvo M, Rodríguez-Moranta F, Taxonera C, Nos P, Mesonero F, Martín-Arranz MD. Increased risk of thiopurine-related adverse events in elderly patients with IBD. Alimentary Pharmacology & Therapeutics. 2019; 50(7):780-788.