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Review Article

Inflammatory Bowel Disease: From a 'White Man's Disease' to a Global Challenge – Exploring Novel Biomarkers and Treatments

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Abstract: Inflammatory bowel disease (IBD) was once labelled a 'White man's disease' due to its ties to industrialized lifestyles, where prolonged exposure to environmental triggers can lead to this debilitating condition over time. From being the disease of developed countries, now it is entwined to developing countries; the only reason behind it is the changes in lifestyle. Treatment options for IBD include 5ASA, TNF alpha inhibitors, cytokine inhibitors, monoclonal antibodies and others. While all these drugs are effective in induction and maintenance phase, no drugs are effective in treating and preventing IBD. Fecal microbiota transplant, probiotics and diet administrations with stem cells have recently developed in treating the disease. There is limited diagnosis available to treat IBD, forcing us to explore new possibilities and approaches to manage and subside IBD along with measures and treatments that prevent the disease from relapsing and recurring. Therefore, here in this review, we have attempted on describing what IBD is, its complications and current treatments available and finally emphasized on the novel biomarkers available or to be in developing stages along with other treatment options available for mitigating the disease including measures that may help prevent IBD from occurring.
Keywords: GCSF: Granulocyte colony stimulating factor, UC: Ulcerative Colitis, CD: Crohn's Disease, TFF: Trefoil factor, HMGB1: High Mobility Group Box 1 Protein.

INTRODUCTION

The gastrointestinal part consists of mouth, esophagus, stomach and the intestines. These need to function properly to absorb the food and nutrients which can be ascribed for survival [1]. One such part of GI tract is the bowel system consisting of the small intestine and the large intestine. When this part of the GI tract is inflamed, it is called Inflammatory Bowel Disease (IBD). It is characterized by 2 diseases: Crohn's Disease (CD) and the Ulcerative Colitis (UD). Ulcerative Colitis is confined to the large intestine whereas, Crohn's disease can affect any part of GI tract from mouth to anus, usually it starts at the base of the stomach and runs down to large intestine [2]. Epidemiology of IBD (presented in table no.1) which was restricted to western countries before and known as white people's disease, now has emerged into Asian countries especially India witnessing a greater number of IBD cases. A lack of good epidemiological studies may have restricted the astute information about the incidence of IBD in India.

Table 1: Survey conducted in India from past 50 years is mentioned below showcasing the incidence of IBD with other Asian countries:

Location	IBD	UC	CD
Hong Kong	2.62	1.25	1.30
Indonesia	0.83	0.27	0.56
Malaysia	1.01	0.18	0.71
Singapore	0.97	0.39	0.51
India	___	6.02	

Despite being a worldwide health issue, Western nations continue to have the highest prevalence. Nonetheless, there has been a noticeable increase in instances in recently industrialized areas of South America, Africa, the Middle East, and Asia. IBD's precise cause and underlying mechanisms are yet

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unknown (Mc Dowell *et al*.,). More than 200 genes linked to IBD susceptibility have been found by genome-wide association studies; some of these genes are involved in the host's immunological response to gut microbiota [3].

Risk Factors for IBD

Once dubbed a "white man's disease," IBD now affects developing nations too: its incidence in industrialized countries has plateaued, while India and China are seeing rises linked to urbanization and economic growth. Chronic GI inflammation reflects a misdirected immune attack shaped by environmental exposures [4], Westernized lifestyles, disrupted circadian rhythms [5], genetic predisposition and immune dysfunction. Smoking increases Crohn's risk but quitting may lower UC risk, although Indian studies find no clear smoking–IBD link; conversely, a vegetarian diet appears protective against UC, suggesting that shifts toward processed foods drive its emergence in emerging economies. Urbanization itself is no longer deemed a risk factor. Globally, UC is strongly associated with gut-microbiota disturbances—from antibiotics, dietary additives and psychiatric comorbidities (Table 2)—with the gut–brain axis further influencing disease progression. Notably, appendectomy seems protective if performed before UC onset but may worsen its course when done afterward [6].

Table 2: Factors affecting IBD

Factors	Western countries	Developing nations
Diet	Processed food (increased risk)	Transitioning to processed (increased risk)
Smoking	Decreased Colitis but increased Crohn's	No significant link (India)
Protective factors	Limited	Vegetarian diet (decreased UC)

Genetic Factors

While external factors are thought to influence the chance of getting UC, genetics have also been linked to the condition. Children of the individuals are more likely to develop UC, which could be due to genetic or environmental factors, or both.

Table 3: Cytokines involved in IBD

Disease	Immune Response	Cytokines
CD	Th 1 and Th 17	IL-1, IL-2, IL17A, IL-17F, IL-18, IL-21, IL-22, IL26
UC	Th 1 and modified Th 2	IL-5, IL-9, IL-13, 1L-17
Both CD and UC	Th 1 and Th 2	IL-6, TNF-α

The majority of the molecular differences between UC and CD includes human leukocyte antigen (HLA) Class II genes, as well as genes related to pattern recognition [e.g., nucleotide-binding oligomerisation domains (NODs) [7].

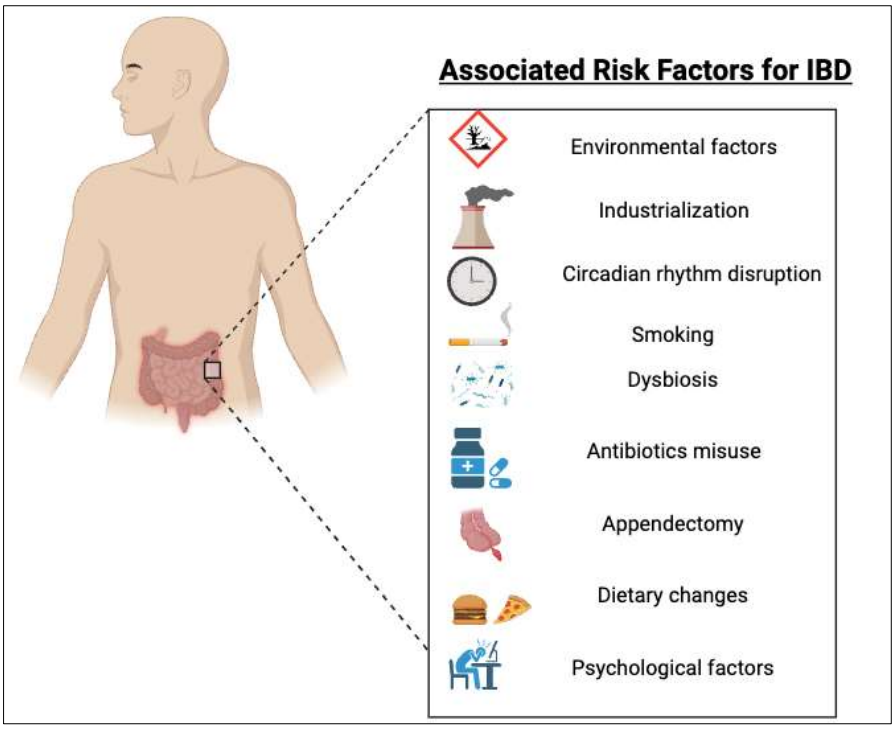


Fig. 1: Risk factors of IBD [7]

Pathophysiology of Ulcerative Colitis

Understanding ulcerative colitis (UC) requires knowledge of the colonic mucosa, which is lined by a single-layer columnar epithelium vital for homeostasis, immune defense, and microbial interaction. Lieberkühn crypts in the mucosa are home to intestinal stem cells that promote fast epithelial regeneration. Enterocytes (absorptive), goblet cells (secreting mucus), Paneth cells, and neuroendocrine cells are examples of specialised epithelial cells. While most cells absorb nutrients, crypt cells secrete them. Colonocytes help absorb electrolytes, whereas goblet cells (~10%) release mucin and immunological mediators (trefoil peptides, RELMβ, FCGBP) to protect against germs. Goblet cells are more abundant in the colon due to its microbial load. Enteroendocrine cells secrete vasoactive intestinal peptide (VIP), which maintains barrier integrity; its dysregulation is linked to colitis susceptibility.

Dysfunction of these epithelial cells disrupts homeostasis, contributing to UC. Histologically, UC shows crypt shortening and reduced branching. Immune cells in the lamina propria, including macrophages, dendritic cells, plasma cells, and lymphocytes, contribute to the pathogenesis of UC together with genetic predisposition [8]. To achieve remission, therapy seeks to restore barrier function by targeting epithelial or immune cells in the lamina propria, respectively.

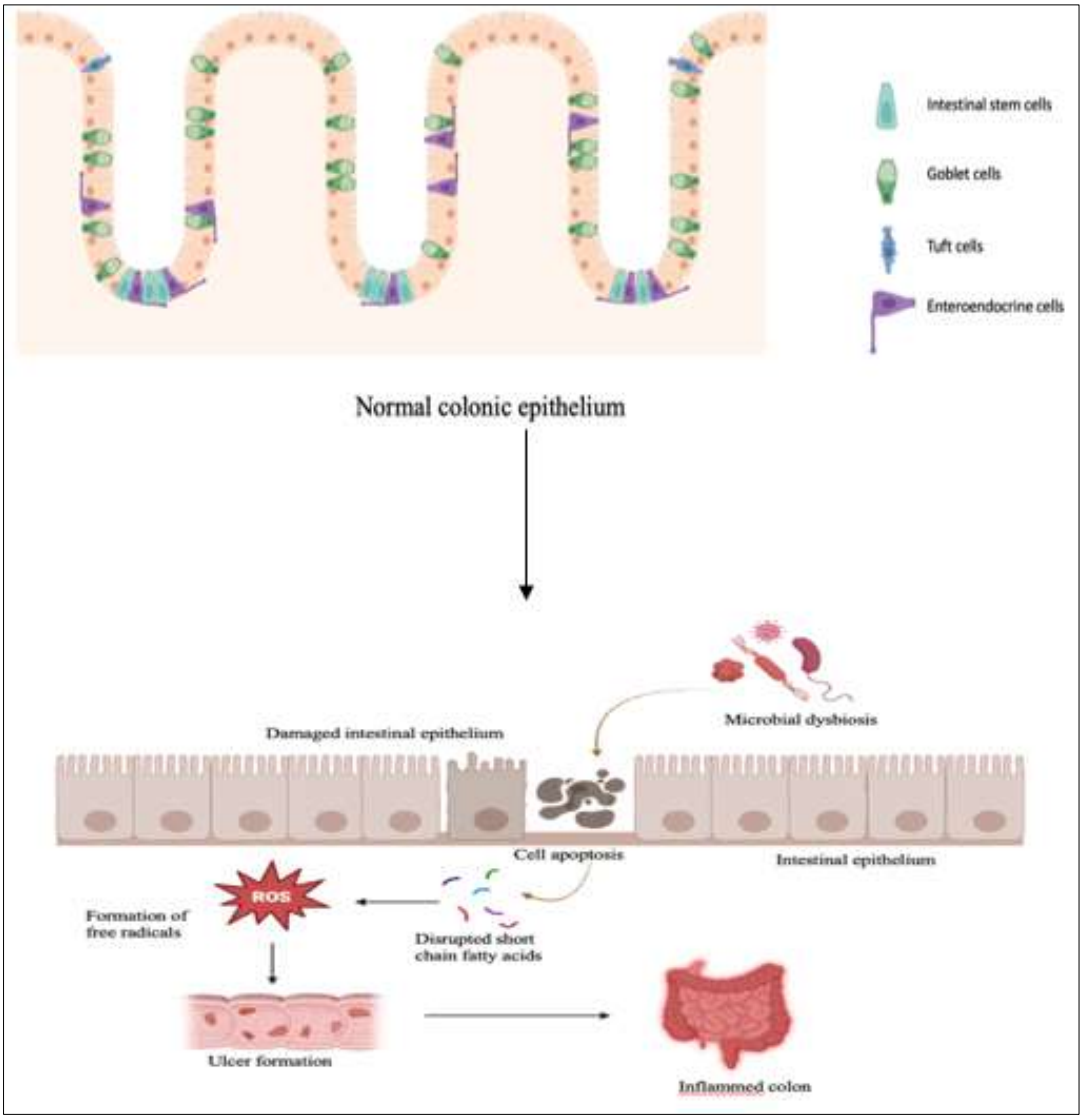


Fig. 2: Pathophysiology of IBD [8]

Gut Microbiome

Gut microbiome or gut flora or microbiota are the collection of microorganisms which are present in the digestive tract of animals. Their number outnumbers by a factor of 10 and their genes outnumber by a factor of 100.

Gut microbiota–derived SCFAs modulate host metabolic activity, nutrient uptake, and energy harvesting [9, 10]. These metabolites have been linked to obesity9 and type 2 diabetes [11]. Both obese adults and children exhibit elevated fecal butyrate and propionate levels compared with lean individuals [12, 13], and shifts

in SCFA concentrations and proportions parallel changes in bacterial phyla [12, 13].

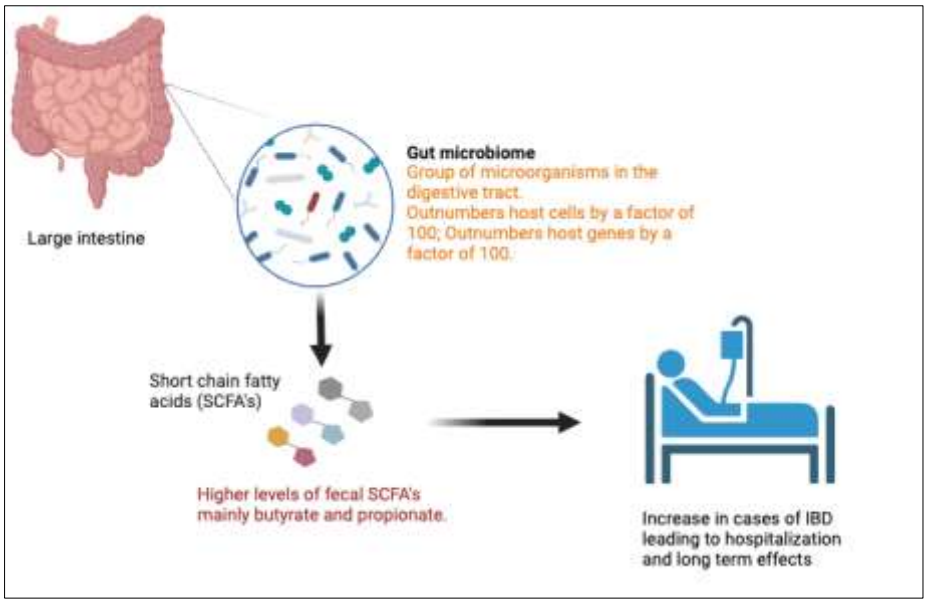


Fig. 3: Gut microbiome in IBD [12, 13]

More than 99% of intestinal bacteria belong to 4 primary phyla: Proteobacteria, Firmicutes, Bacteroidetes and Actinobacteria. Among these, Bacteroidetes and Firmicutes are the most predominant in a healthy gut microbiome. The gut microbiota in healthy people—whose composition and abundance fluctuate spatially along the gastrointestinal system (Fig. 4)—supports pathogen defence, food digestion, metabolism, and immunological function through dynamic, symbiotic interactions. Dysbiosis, or alteration of this community's composition and function, is common in IBD and IBS, but its exact role—whether it triggers immune activation and inflammation or derives from it—is unknown. While the microbiota is normally stable over time, it can be affected by diet, environment, infections, lifestyle, and drugs; in IBD, such dysbiosis affects host immunological and metabolic processes as they strive to re-establish equilibrium.

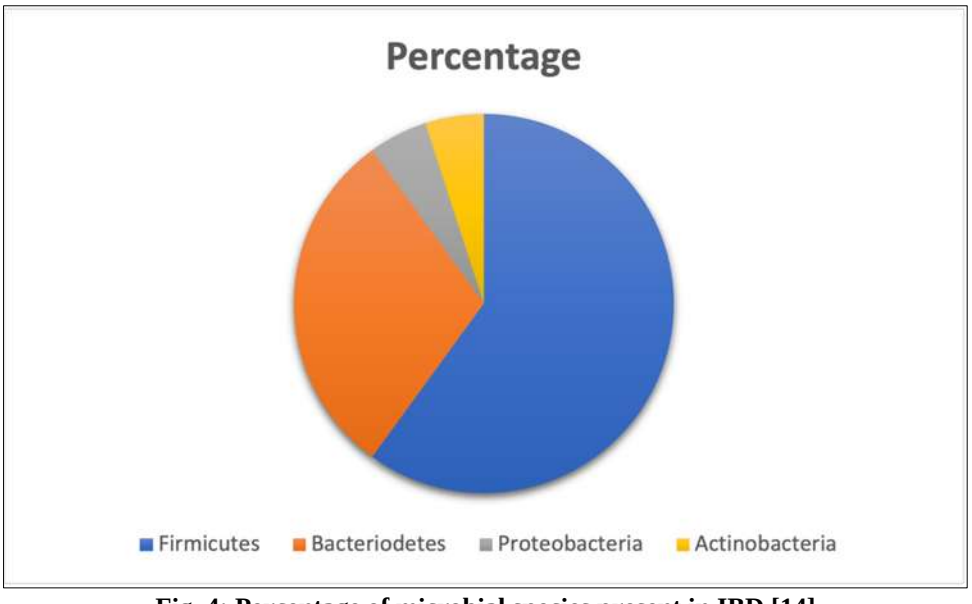


Fig. 4: Percentage of microbial species present in IBD [14]

Missing clinical metadata and insufficient taxonomic precision of 16S rRNA amplicon sequencing hinder mechanistic insights into IBD-associated microbiome changes. This restricts analysis to family or genus level and fails to capture interindividual variability. Moreover, 16S ASVs lack functional information essential for understanding host–microbe interactions. Integrating higher-resolution metagenomics, metatranscriptomics, and metabolomics with comprehensive host metadata—such as clinical

progression, medication use, mucosal gene expression, histology, and immunological markers—provides a much richer, systems-level perspective into both health and disease states [14].

Interactions between microbial composition, immunological modulation, and environmental factors are all part of the intensee relationship between the gut microbiome and the development of IBD. IBD is caused by a confluence of microbial imbalances, environmental triggers, and genetic predispositions. Each of these factors has a role in the development and progression of the disease. The gut microbe dysbiosis, is a key feature of IBD. Reduced microbial diversity is often observed in IBD patients, as evidenced by an increase in potentially harmful bacteria, especially those belonging to the Proteobacteria phylum, and a decrease in helpful bacteria, such as Firmicutes. It is still unknown, though, if dysbiosis results from the illness or if it causes immunological activation and inflammation.

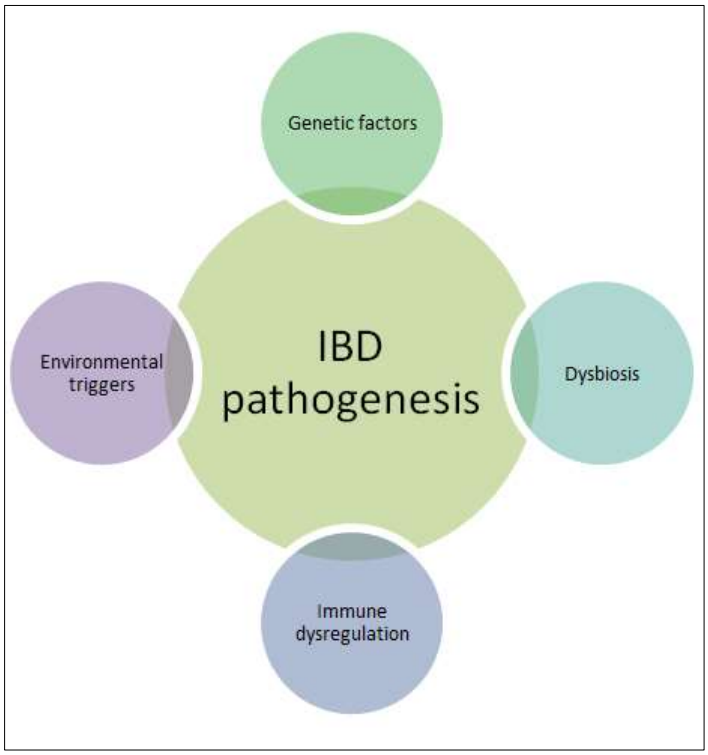


Fig. 5: Different triggers of IBD

The gut microbiota regulates immune responses and maintains intestinal health. Microbial metabolites, such as short-chain fatty acids (SCFAs), secondary bile acids, and amino acid catabolites, help maintain the intestinal barrier. For example, butyrate, a SCFA generated by Firmicutes, improves intestinal barrier integrity and has anti-inflammatory characteristics. A decline in butyrate-producing bacteria in IBD patients causes increased intestinal permeability and chronic inflammation. Similarly, changes in bile acid metabolism and amino acid-derived substances might impair immunological signalling, resulting in excessive inflammation. Several host variables influence gut microbiota composition and function. Genetic variations in genes involved in microbial detection, immunological regulation, and gut barrier maintenance can increase vulnerability to IBD.

Prebiotics And Its Effect on Gut Microbiota

Prebiotics; non-digestible food substances that regulate the gut microbiota by selectively increasing the growth and activity of helpful bacteria like Bifidobacterium and Lactobacillus spp. These bacteria support gut homeostasis by producing SCFA's such as acetate, propionate and butyrate that aid in gut barrier integrity and inflammatory regulation. Prebiotics can improve IBD by increasing the number of *Faecalibacterium prausnitzii*, a major butyrate generator, and decreasing pro-inflammatory cytokines such as TNF-α and IL-1α. Oligofructose-enriched inulin (OF-IN) has been shown to modify gut microbiota composition, benefiting patients with CD and UC. Prebiotics also influence metabolic health by altering the Firmicutes/Bacteroidetes ratio, which is frequently dysregulated in hyperlipidemia and metabolic syndrome, as well as by controlling appetite hormones such as ghrelin and leptin, all of which contribute to enhanced metabolic function. Beyond gut health, prebiotics have been linked to cognitive benefits, decreased anxiety and depression, and improved immunological responses, making them potential therapeutic agents for a variety of health issues [2].

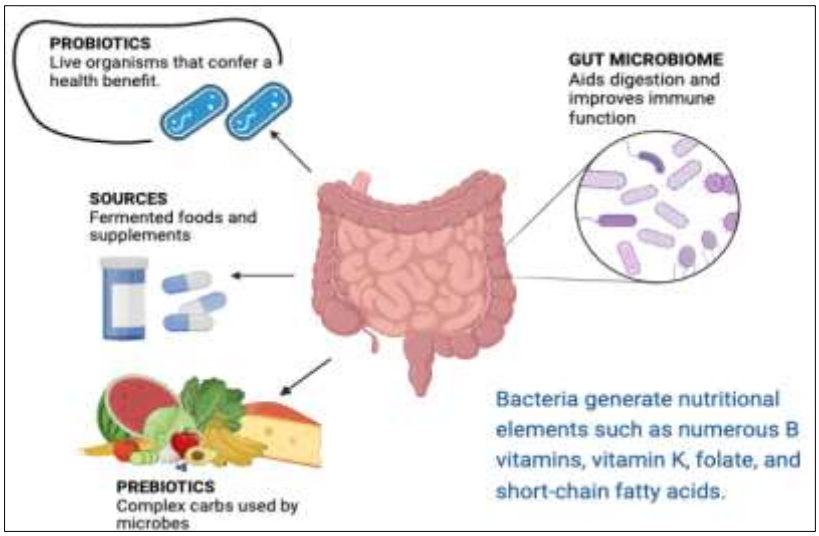


Fig. 6: Probiotics in gut microbiome

Probiotics

Probiotics are "live microorganisms that, when administered in adequate amounts, confer a health benefit on the host" as described by International Scientific Association for Prebiotics and Probiotics. Current definitions state that probiotics have to survive in alimentary canal where they exert their benefits [15]. These microorganisms, predominantly bacteria but also yeasts, occur naturally in fermented foods, can be added to other foods, and are available as nutritious supplements. However, not all probiotic-labeled foods and nutritional supplements on the market have been demonstrated to improve health. Probiotics should not be confused with prebiotics, which are complex carbohydrates (like pectin and other galacto-oligosaccharides) that microorganisms in the gastrointestinal system need for metabolic fuel. Synbiotics contain both probiotic microbes and prebiotic carbohydrates.

To understand the possible impact of probiotics on health, first we need to understand the functions of the normal gut microbiome (commensal microbiota). The human GI contains approximately 500 bacterial species and lesser-known virome. These bacteria act as virtual bioreactor that aids digestion, nutrition, and immune system development. Our intestinal bacteria can weigh up to 1kilogram, and bacterial cells outnumber human cells ten times more than the intestinal bacteria[8]. The bacterial genome may outnumber the human genome by a hundred to one. These bacteria produce a variety of nutritional elements, including B complex vitamins, K vitamin, folate, and short chain fatty acids. Bacterial fermentation byproducts can satisfy up to 10% of an individual's daily energy needs [16].

Biomarkers in Ulcerative Colitis

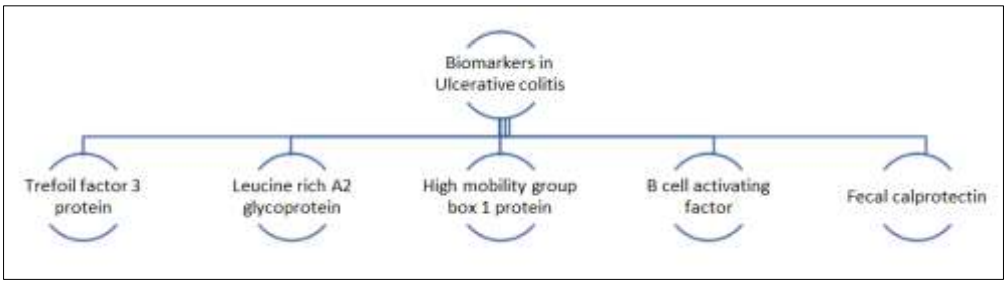


Fig. 7: Biomarkers in Ulcerative colitis

For UC, there isn't yet a single "gold standard" diagnostic test. Rather, a mix of parameters including histopathology are used to make the diagnosis [17]. Unfortunately, diagnostic uncertainty can occasionally arise from tests performed by skilled medical professionals [18-20].

Trefoil Factor 3:

The intestinal mucosa's goblet cells secrete a series of three mucin-associated peptides known as trefoil factors [21]. They are increased at the site of mucosal injury and are crucial for preserving the integrity of mucosal barrier [22, 23]. The gastrointestinal mucosa is shielded against various assaults by TFF3 [24], often referred to as intestinal trefoil factor, which is mostly released by goblet cells in the small and large intestine [21].

When administered exogenously after enteral or parenteral administration, TFFs have been demonstrated

in vivo to have protective and healing properties. This research raises the possibility that TFFs could help treat IBD. Here, mouse colitis models have proven helpful in investigating the connection between intestinal damage and TFF expression, and consequently, the function of exogenously supplied TFFs in epithelial repair in cases of mucosal injury. Following oral injection of dextran sulphate sodium (DSS), a chemical that produces mild epithelial injury in wild-type mice, Mashimo *et al.,* [25], demonstrated that mice lacking TFF3 had poor epithelium regeneration following injury and impeded mucosal healing. These mice perished from severe colitis. After radiation and chemotherapy-induced damage, the same thing was observed[26]. Furthermore, TFF3-knockout mice subjected to radiation-induced damage and DSS were able to regain their ability to repair after receiving luminal therapy with recombinant TFF3 (rTFF3) [25, 26].

Surprisingly, TFF3 and CRP levels in UC patients correlate well. When combined, they have a predictability of complete MH that is comparable to FC. This allows UC patients to forego stool collection and can be monitored solely with blood testing [27].

Leucine-Rich Alpha-2 Glycoprotein

Leucine-rich alpha-2 glycoprotein (LRG) is a new serum biomarker for a number of illnesses that was discovered in rheumatoid arthritis patients utilising a proteomics technique [28]. Numerous autoimmune disorders have been found to have higher serum LRG levels, with higher levels in SLE, arthritis and IBD [28-35]. LRG is produced in the liver and in inflammatory tissues, and its overexpression is linked to IL-6, IL-1β, TNFα, IL-22, and other proteins [36, 37]. According to earlier research, serum LRG levels had a stronger correlation with UC disease activity than CRP [30-32].

According to research with 129 UC patients, those with active disease had considerably higher serum LRG levels than those in remission. Additionally, also in patients with normal CRP levels, there was a strong correlation between LRG levels and endoscopic activity [31].

Hepatocytes, macrophages, neutrophils and epithelial lining of intestines, all express LRG. Instead of IL-6, which is the primary factor driving the creation of CRP, inflammatory cytokines such as IL-22, TNF-α, and IL-1β impact its induction [30,31]. Patients who achieved complete mucosal healing (CMH) had considerably lower LRG levels than patients with active illness when mucosal healing was measured [38]. Serial LRG assessments in a longitudinal follow-up showed variations in endoscopic status, with lower levels following mucosal repair and greater levels during active disease. Furthermore, compared to CRP, LRG demonstrated greater sensitivity and specificity in identifying mucosal healing, according to receiver operating characteristic (ROC) analysis [30-32].

All things considered, LRG is a useful biomarker for UC that may identify disease activity, direct therapy choices, and forecast therapeutic results, making it a crucial instrument in clinical care.

HMGB1 Protein:

High-mobility group box 1 (HMGB1), which originally demonstrated the ability to bind DNA, also has strong proinflammatory effects [39-41]. By partially activating the receptor for advanced glycation end products (RAGE), exposure to HMGB1 causes neutrophils or macrophages to produce more pro-inflammatory cytokines, such as TNF-∝ and IL-1, causes nuclear translocation of NF-κB [42-44].

Blocking HMGB1 with certain antibodies increases survival and inflammation while decreasing pro-inflammatory cytokines in the blood. HMGB1 affects animal models of inflammation, including endotoxemia, peritonitis, hepatic injury, and lung injury [45-48]. However, not much is understood about how HMGB1 contributes to colonic damage.

Thirty to eighty-three percent of individuals with ulcerative colitis (UC) have sera that include perinuclear anti-neutrophil cytoplasmic antibodies (P-ANCA), which are thought to be a diagnostic marker for UC and help differentiate it from CD [49]. UC patients' serum contains anti-HMG1/HMG2 antibodies, which have been shown to be substantially correlated with disease activity.

Added to that, faecal HMGB1 exhibits a substantial correlation with the level of Geboes histological score of inflammation in UC patients who have both clinical and endoscopic remission [50, 51]. As a result, HMGB1 can be used as a non-invasive biomarker of mucosal repair and clinically overt subclinical gut inflammation, highlighting its potential utility in tracking disease development and assessing therapy efficacy [52]. In clinical practice, faecal HMGB1 can be used to detect histological changes in persons with endoscopic and clinical remission, as well as to serve as a reliable biomarker of intestinal inflammation in both paediatric and adult UC patients.

BAFF:

BAFF is a member of the tumour necrosis factor (TNF) superfamily that has lately emerged as a potential drug candidate for IBD [53]. The primary function of BAFF, which is mostly released by myeloid cells is to regulate the survival of mature B cells and their maturation into plasma cells that make antibodies. BAFF is a type-II transmembrane protein of 285 amino acids that belongs to the TNF superfamily (TNFSF-13B). A furin protease can cleave surface-bound BAFF, producing a soluble, 17-kDa protein with 152 amino acids [54].

Dendritic cells, macrophages, monocytes and a subset of T lymphocytes are among the immune cells that express and release BAFF [54-57]. Numerous cytokines like interleukin (IL)-10, GCSF, interferon-γ and Toll-like receptor activation can raise the production of BAFF [58, 59]. BAFF expression promotes humoral immune system activation and sustains continuing immunological responses when triggered by pro-inflammatory cytokines. Furthermore, non-myeloid radiation-resistant cells—likely stromal cells like osteoclasts—produce a sizable portion of the circulating BAFF [60].

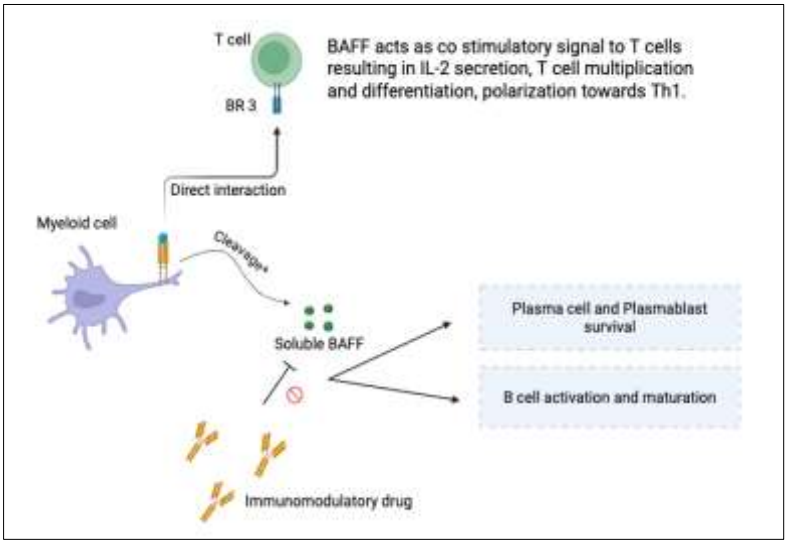


Fig. 8: BAFF action [65]

Data from colonic biopsies from CD and UC patients show that BAFF contributes to IBD pathogenesis due to elevated mRNA and BAFF protein expression levels. BAFF was primarily upregulated in lamina propria mononuclear cells in inflammatory areas of the UC mucosa [61]. Gastrointestinal macrophages and dendritic cells produced from monocytes have significant interactions with the microbial environment, proinflammatory tissue damage, adaptive immune response induction, and mucosal inflammation resolution [62]. While Th2 responses predominate in the pathobiology of UC, Th1 responses appear to be the primary driver of inflammation in CD [63]. However, other lymphocytes have also emerged as important contributors to the pathophysiology of IBD, including Th17 cells and innate lymphoid cells [64].

Fecal Calprotectin:

Calprotectin is an alarmin, an antibacterial agent, and a dimer of the proteins S100A8 and S100A9 that chelates iron and zinc [66]. When inflammation starts, the colon releases this protein, which is among the most prevalent in neutrophils. Calprotectin is a handy, non-invasive biomarker with a higher diagnostic value than the faecal immunochemical test due to its high stability in faeces [67, 68]. According to an IBD study, calprotectin levels were considerably higher in faeces of IBD patients, and the degree of elevation was positively connected with the disease's severity [69].

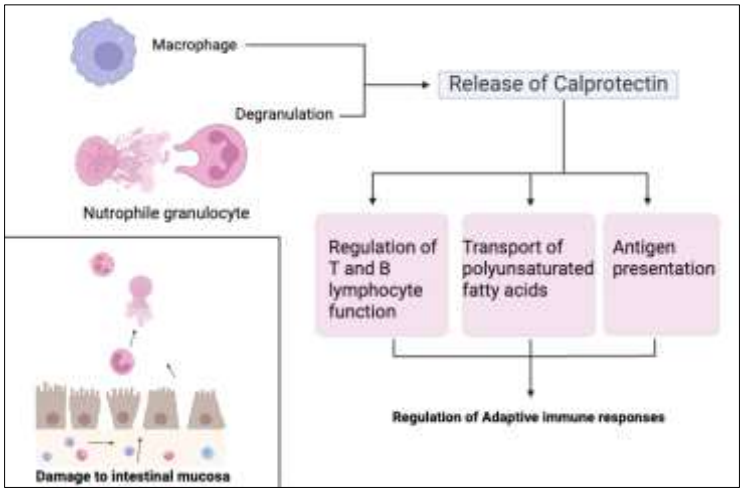


Fig. 9: Calprotectin involvement in IBD and Pathophysiology [70]

Calprotectin reduces intestinal inflammation by inducing the release of anti-inflammatory mediators when the intestinal tract becomes infected or inflamed [71]. This anti-inflammatory impact is important for maintaining the intestinal barrier's structural integrity and avoiding inflammation-induced barrier degradation.

Current Therapies in Ulcerative Colitis

According to the severity of ulcers the management of colitis can be classified. Mainstream therapy for Ulcerative Colitis:

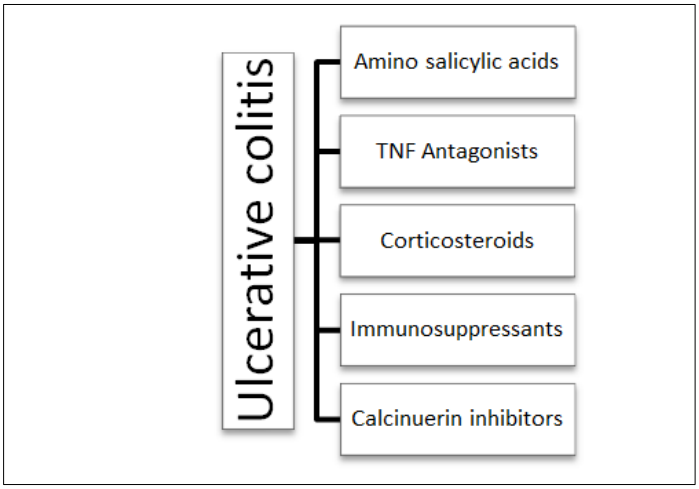


Fig. 10: Current therapies in UC

Aminosalicylic Acid Derivatives:

5-aminosalicylic acid is a first-line medication for UC that is successful in causing and sustaining remission [72, 73]. For proctitis, topical mesalamine is recommended; suppositories provide superior medication administration to the rectal cavity [72]. Oral formulations target severe colitis, while rectal mesalamine is advised for proctitis/left-sided colitis. Although several forms of mesalamine act on different parts of the gut, no formulation has proven to be better than the others. Oral plus topical medication is best for mild-to-moderate pancolitis or left-sided colitis, and combination therapy with topical steroids improves results [74].

TNF Antagonists:

An inflammatory cytokine, TNF-α plays a role in lymphoid organ development, bone metabolism, T-B Lymphocytes, inflammation, apoptosis, lymphocyte stimulation, and immune cell activation. The most significant cytokine mediating intestinal tract inflammation is TNF-α, and IBD is associated with increased TNF-α expression [75].

Several modest trials have demonstrated that in patients who have experienced a subordinate loss of response to a first TNF inhibitor, switching between TNF inhibitors can be an effective therapy approach [76-78]. The findings are corroborated by the results of the ENEIDA Registry, which showed that while 55% of patients who switched to a second TNF inhibitor after failing or becoming intolerant to a previous TNF inhibitor experienced short-term remission, a percentage of them later experienced further loss of response[78]. Additionally, two systematic studies advocate for moving on to a second TNF inhibitor once treatment fails [79].

Corticosteroids:

The finding that corticosteroids were beneficial in UC significantly improved a condition that had previously had a high death rate. The mortality rate decreased from 61% to 4–7% [80, 81].

Route of Administration	ORAL	INTRAVENOUS	RECTAL
Medications	Cortisone Prednisone Prednisolone Budesonide	Prednisolone Methylprednisolone Corticotropin	Beclomethasone Budesonide Prednisolone Tixicortol Metasulfobenzoate

In 1955, Truelove and Witts reported that 100 mg of cortisone per day was effective in treating UC [82]. Left-sided UC responds well to rectal corticosteroids. For individuals suffering from haemorrhage and tenesmus, they offer prompt relief. Controlled trials have shown that rectal hydrocortisone 100 mg and prednisolone 10 mg can induce remission but not maintain it [83-86].

Immunosuppressants:

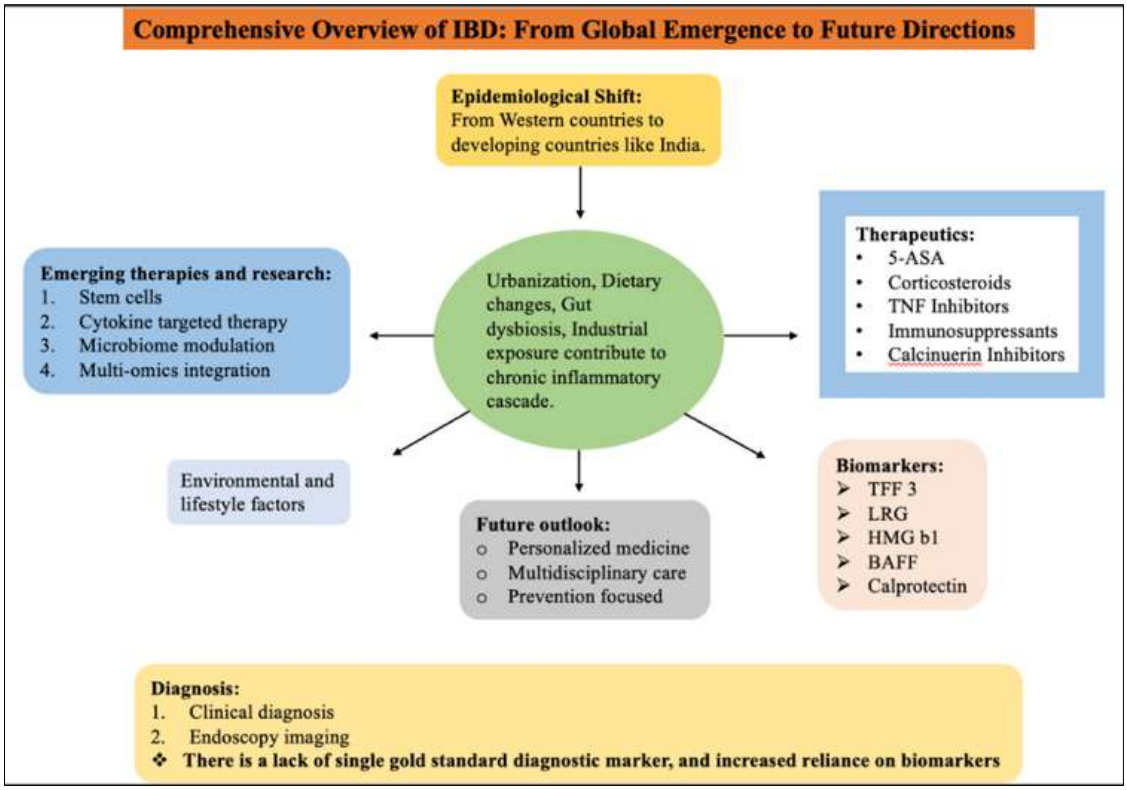
An immunosuppressant is a type of medication that inhibits or reduces the body's immunological response. Most of these medications are designed to weaken the body to fight a replaced organ, such as a kidney, heart, or liver [87-91]. Immunosuppressive medications or immunosuppressants are classified into four broad categories: glucocorticoids, protein drugs, intravenous gamma globulin, and protease inhibitors. Each class is then divided into subclasses [92].

6-Mercaptopurine and its prodrug Azathioprine are purine antimetabolites that have the ability to induce and maintain UC remission while sparing steroids [93]. Several uncontrolled research verified their effectiveness, despite other studies' contradictory findings.

Azathioprine and 6-Mercaptopurine recommended; complete effects may take up to 17 weeks. With lower dosages for patients with intermediate enzyme activity and contraindications for those without TPMT activity, TPMT testing aids in the determination of safe dosage. Pancreatitis, rash, nausea, and hepatitis are examples of allergic reactions (5%) and nonallergic consequences include anaemia, opportunistic infections, and bone marrow suppression.

Calcinuerin Inhibitors:

Calcineurin inhibitors such as cyclosporine-A (CyA) and tacrolimus offer non-surgical options for severe or refractory ulcerative colitis (UC). In a meta-analysis of randomized trials, CyA significantly improved remission rates versus placebo or no treatment [94]. Intravenous CyA (4 mg/kg) induces remission within 5–7 days, but long-term efficacy is unclear and its use is limited by nephrotoxicity, neurotoxicity, and opportunistic infections—3.5% mortality from infections like Aspergillus and Pneumocystis pneumonia has been reported [95]. Tacrolimus has also shown promise: in a randomized trial, high-dose tacrolimus (10–15 ng/mL) improved clinical outcomes in 68.4% of patients versus 10% with placebo ($p < 0.001$), reduced steroid dependence, and achieved 20% remission; finger tremors were the most common side effect, with higher adverse events at elevated doses [96]. For UC patients who do not react to standard therapies, tacrolimus and CyA are also viable options that may avoid surgery. However, due of the risk of serious adverse effects, its use should be continuously monitored. More research is needed to determine the best dose regimes, long-term benefits, and how to integrate these medications into UC treatment protocols.



CONCLUSION

Inflammatory bowel disease (IBD) is now a global issue—including in India—driven by urbanization, Westernized diets, lifestyle shifts, and environmental stressors. It features chronic, relapsing gut inflammation due to immune dysregulation, genetic susceptibility, environmental triggers, and microbiota imbalance. While immunosuppressants, corticosteroids, aminosalicylates, and biologics can induce and maintain remission, they often fail to fully heal mucosa or prevent

relapse and carry long-term risks. Dysbiosis in IBD has spurred adjunctive microbial therapies (prebiotics, probiotics, fecal microbiota transplantation) alongside dietary and psychological support. Novel noninvasive biomarkers—fecal calprotectin, trefoil factor 3 (TFF3), HMGB1, BAFF, and LRG—offer promise for treatment guidance and earlier, personalized intervention. Optimal management thus integrates conventional treatments, advanced diagnostics, lifestyle modification, public-health measures, and precision medicine to improve outcomes.

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