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REVIEW

Gut microbiome diversity in acute infective and chronic inflammatory gastrointestinal diseases in North India

Saurabh Kedia[1] · Ritika Rampal[1] · Jaishree Paul[2] · Vineet Ahuja[1]

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Abstract The disease profile in the Indian population provides a unique opportunity for studying the host microbiome interaction in both infectious (amebiasis) and autoimmune diseases like inflammatory bowel disease (IBD) from a similar environment and genetic background. Analysis of fecal samples from untreated amebic liver abscess (ALA) patients, *Entamoeba histolytica* (Eh)-negative and -positive asymptomatic individuals, and pus samples from naive ALA patients revealed a significant reduction in *Lactobacillus* in asymptomatic individuals (Eh +ve) and ALA patients. Two anaerobic genera, namely *Bacteroides* and *Peptostreptococcus*, were detected in naive ALA pus samples. Analysis of fecal samples from amoebic colitis patients showed a significant decline in population of *Bacteroides*, *Clostridium coccoides* and *leptum* subgroup, *Lactobacillus*, *Campylobacter*, and *Eubacterium,* whereas a significant increase in *Bifidobacterium* was observed. Mucosa-associated bacterial flora analysis from IBD patients and healthy controls revealed a significant difference in concentration of bacteria among predominating and subdominating genera between ulcerative colitis (UC), Crohn's disease (CD) patients, and controls. In contrast to the mucosal studies, we found a significant increase in *lactobacilli* population in fecal samples of active UC patients. Another study revealed a significant decrease of *Clostridium coccoides* and *leptum* clusters in fecal samples of active UC patients along with decreased concentrations of fecal SCFAs, especially of *n*-butyrate, iso-butyrate, and acetate. We therefore found similar perturbations in gut microbiome in both infectious and autoimmune diseases, indicating inflammation to be the major driver for changes in gut microbiome.

Keywords Gut microbiome · Amebiasis · Amoebic liver abscess · Ulcerative colitis · Crohn's disease

Introduction

The human gut harbors more than 10^{14} microorganisms, comprising more than 500–1000 species [1–3]. These include bacterial, microeukaryotic, and viral populations [4]. The human gastrointestinal tract and these microbiota form a unique ecosystem, and this association of host and microbiome contributes to both health and disease status of the host. The interaction between host and gut microbiome starts right from birth and continues throughout the life. The microbiota colonize the gut soon after birth and the mother of the host is the first source for these gut microbiota [5, 6]. A number of factors, including diet [7–9], age [10], gender, genetic composition [11], geographic location [2], and health/disease status [6] of the individual influence the gut microbiota after birth. The microbiota varies in their diversity and stability with advancing age. In early life, the microbiome is characterized by low diversity and low stability [12] and the microbiome gains stability and diversity by early adulthood [13, 14] (Fig. 1). Metagenome refers to the genetic contents of entire microbial community residing in the human gut. Metagenome of the human gut colonizers has more than 100 times the number of genes as compared to human genome [15]. The greatest population density of these microbes is observed in distal

✉ Vineet Ahuja
vineet.aiims@gmail.com

[1] Department of Gastroenterology, All India Institute of Medical Sciences, New Delhi, India

[2] School of Life Sciences, Jawaharlal Nehru University, New Delhi, India

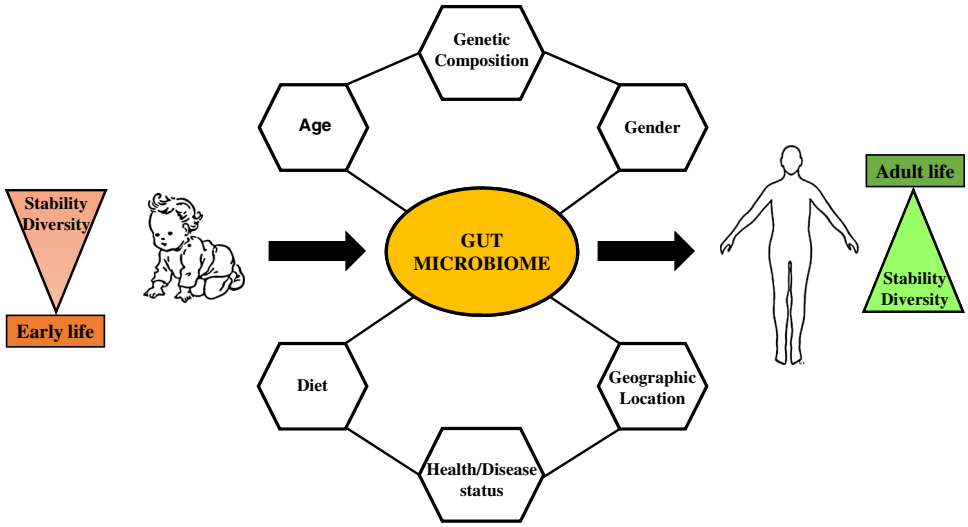

Fig. 1 Factors affecting gut microbial diversity and stability

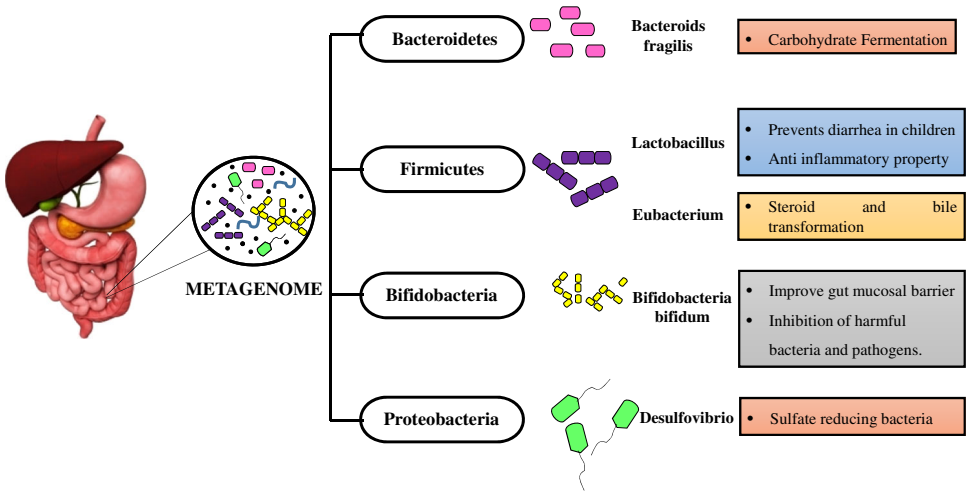

Fig. 2 Major bacterial constituents of gut metagenome

ileum and colon [1]. The predominant microbial flora of human GI tract includes the following phyla: *Bacteroidetes, Firmicutes, Proteobacteria* (includes *Enterobacteriaceae*), *Actinobacteria, Fusobacteria*, and *Verrucomicrobium* (Fig. 2). Of these, *Firmicutes* and *Bacteroides* form more than 90 % of the bacterial population present in the colon [16].

- *Bacteroides* species of the *Bacteroidetes* phylum are the most dominant species, and are predominant starch degraders. They play a very important role in carbohydrate metabolism, nutrition, and maintenance of health [17].
- *Eubacterium* genus of the *Firmicutes* phylum is the second most dominant species. The members of the genus *Eubacterium* are known to produce butyrate [18], degrade flavonoids (from vegetables, fruits, nuts, and tea) [19], and are implicated in steroid and bile transformation in intestine. Other members include *Clostridium* group IV and XIVa, which are predominant butyrate-producing strains [20]. Non-butyrate-producing members include *Ruminococcus torques* and *R. gnavus*, which are among the primary mucin-degrading organisms [21]. The genus *Lactobacillus*, comprising a large heterogenous group of low G + C Gram-positive, non-sporulating, anaerobic bacteria and are other important members of the phylum *Firmicutes*. *Lactobacilli* are known to fortify the epithelial barrier by various mechanisms such as induction of mucin secretion, enhancement of tight-junction functioning, upregulation of cytoprotective heat shock proteins, and prevention of apoptosis of epithelial cells [22]. Probiotic strains of *Lactobacillus* are known to prevent infectious diarrhea, antibiotic-associated diarrhea, and diarrhea in children who are unusually more susceptible as a result of poor nutrition, impaired immune status, or frequent exposure to pathogens [23].

- Members of *Bifidobacteria* (member of *Actinobacteria* phylum) produce acetate in proximal and distal colon by fermentation of glucose and fructose [24]. Members of both *Bifidobacteria* and *Ruminococcus* (*Ruminococcus torques* and *Bifidobacterium bifidum*) are thought to ferment mucin and compete to colonize this substrate for their energy source [25].
- Sulfate-reducing bacteria are found in five distinct genera in the delta subdivision of the *Proteobacteria* phylum [26]. Hydrogen-consuming, sulfate-reducing bacteria are found in two of these genera, e.g., *Desulfovibrio* [27].

Of the above-mentioned bacteria, *Bacteroides, Bifidobacterium, Eubacterium, Clostridium, Peptococcus, Peptostreptococcus, Lactobacillus*, and *Ruminococcus* are considered to be predominant genera, whereas *Enterococcus, Methanobrevibacter*, and sulphur-reducing bacteria (SRB) remain as the subdominant genera [28]. Both the host and gut microbiota benefit each other as microbes benefit from the nutrient-rich host GI tract and the host benefits from the metabolic abilities of the microbes. The beneficial effects of these microbiota (which form a 'microbial organ' within the intestine) [29] are mentioned in the Fig. 3.

Gut microbiome in both health and disease are currently under intense investigation worldwide by scientists and clinicians with diverse expertise and interests. We present our experience of interrogating gut microbiome, looking at changes in its diversity and composition in gut parasitic diseases like amebiasis, which are very prevalent in tropical countries and in organ-specific auto-immune diseases like inflammatory bowel disease (IBD), which is rapidly emerging in the tropical countries.

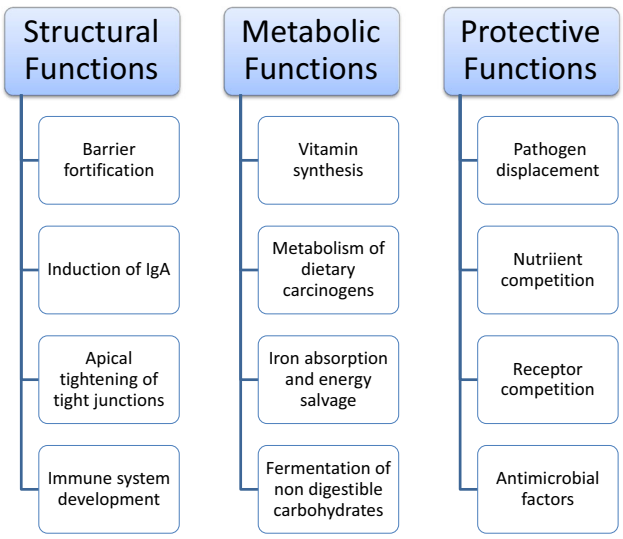

Fig. 3 Gut microbiome functions in human health

Intestinal flora and amebiasis

Entamoeba histolytica is a micro-aerophilic protozoan that is the causative agent of invasive amebiasis, including colitis and liver abscess. It is still a significant cause of morbidity and mortality in developing countries like India [30]. Although both the protozoan and intestinal flora reside together in the gut, their interaction and the contribution of gut flora towards the manifestation of invasive amebiasis is not well understood. Amebiasis is initiated with ingestion of *E. histolytica* cysts through fecally contaminated water/food. Trophozoites are released after excystation of these cysts in the intestinal lumen. After infection in most of the individuals, these trophozoites usually live as commensals without causing any damage to the host, and very few individuals develop invasive disease [31]. India is endemic for amebiasis, and the total number of infected individuals is very high (up to 20 % of the Indian population). These trophozoites initiate invasive disease when they penetrate the mucus layer and damage the intestinal tissues [32, 33]. The trophozoites drive their nutrition by ingesting intestinal flora [34]. The bacterial flora also provides anaerobic conditions or low redox potential, which is beneficial for amoebic growth [35]. However, the amoeba are very selective in their interaction with the different bacterial species, and only those bacteria that have appropriate receptors are ingested by these trophozoites [36]. It has also been proposed that intestinal flora may also influence the virulence potential of *Entamoeba*, as certain bacterial species may trigger virulence while others my decrease it [37]. Fluctuations in gut flora have been reported in acute diarrhea and antibiotic-associated diarrhea [33]. However, little was known about the *Entamoeba*–gut flora cross talk. Therefore, our group studied the clinical correlation between resident bacterial flora and severity and spectrum of amoebic disease.

In a collaborative study [38], we looked into the profile of predominant gut flora of healthy individuals, asymptomatic *E. histolytica* carriers, and amebic liver abscess patients. We also addressed the issue of whether the changes observed in the gut flora may be attributed to the administration of metronidazole or the presence of the parasite. We also looked for the presence of gut bacteria in the liver abscess aspirates. The prevalence of the metronidazole-resistance gene (*nim*) was also scored in these bacterial species. Stool samples were analyzed from the following categories of individuals: (1) healthy *E. histolytica*-negative (2) healthy, asymptomatic, *E. histolytica*-positive, and (3) amoebic liver abscess (ALA) patients. Pus samples were also analyzed from ALA patients for the presence of 11 prominent, mostly anaerobic, bacteria found in the human gut. Bacterial detection was done by PCR

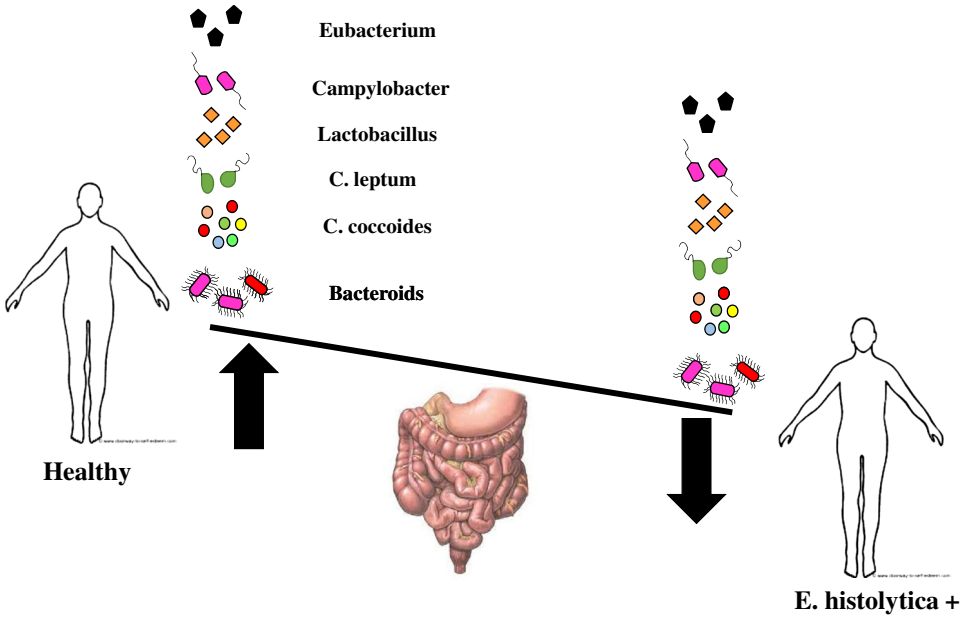

Fig. 4 Dysbiosis in *Entamoeba histolytica* colitis as compared to healthy individuals

amplification of total DNA from samples, using genus-specific primers for the 16S rRNA gene. The specificity of detection was ascertained by sequencing the PCR-amplified bands and confirming their identity by comparing with genus-specific sequences available in the database. There was a statistically significant drop in the frequency of four of the 11 bacterial genera, namely, *Bacteroides*, *Bifidobacterium*, *Lactobacillus*, and *Clostridium* in fecal samples of ALA patients when compared with healthy, *E. histolytica*–negative controls (Fig. 4). Of these, three genera (*Bacteroides*, *Bifidobacterium*, and *Clostridium*) were not reduced in healthy asymptomatic carriers (*E. histolytica*-positive) compared with healthy *E. histolytica*–negative individuals. However, *Lactobacillus* was reduced in *E. histolytica*–asymptomatic carriers also. Asymptomatic carriers also showed a statistically significant decrease in the incidence of *E. coli* and increase in *Pseudomonas aeruginosa* compared with the other two categories of individuals. No significant changes were observed for *Peptostreptococcus productus*, *Ruminococcus*, *Campylobacter*, and *Peptococcus* among healthy controls and ALA patients (Table 1).

Patients with ALA were on metronidazole for ethical reasons while *E. histolytica*-positive asymptomatic carriers did not receive metronidazole. This could account for the observed reduction in *Bacteroides, Bifidobacterium*, and *Clostridium* in ALA patients alone [39]. On the other hand, *Lactobacillus* was reduced in both ALA patients and asymptomatic *E. histolytica* carriers possibly due to *Entamoeba* infection.

We confirmed the effect of metronidazole on intestinal flora by testing healthy volunteers (residents of an urban area) and irritable bowel syndrome (IBS) patients before and after taking metronidazole (Table 2). We observed

Table 1 Prevalence of selected bacteria in fecal samples from healthy individuals and ALA patients

Bacterial species	*E. histolytica* negative ($n = 19$)	*E. histolytica* positive ($n = 11$)	Patients with amoebic liver abscess ($n = 19$)	Significant p value
Bifidobacteria	16	8	4	Gr [#] I vs. Gr III
Clostridium	14	8	4	Gr I vs. Gr III
Ruminococcus	17	7	12	
Campylobacter	7	7	10	
Pseudomonas	6	10	7	
Lactobacillus	18	4	3	Gr I vs. Gr 2 vs. Gr 3
Peptococcus	12	9	8	
Bacteroides	12	9	3	Gr I vs. Gr III
Peptostreptococcus	12	10	14	

Gr[#]: Group, Gr I *E. histolytica negative* patients, Gr II *E. histolytica* positive patients, Gr III: Patients with amoebic liver abscess

Table 2 Effect of metronidazole on the prevalence of selected bacteria in fecal samples in healthy Individuals

Bacterial species	Pre metronidazole ($n = 11$)	Post metronidazole ($n = 11$)	p value
Bifidobacteria	11	4	0.0039
Clostridium	11	5	0.0124
Ruminococcus	10	5	ns
Campylobacter	9	1	0.0019
Pseudomonas	7	4	ns
Lactobacillus	11	11	ns
Peptococcus	11	6	0.035
Bacteroides	11	2	0.002
Peptostreptococcus	11	8	ns

similar results and found that there was a marked drop in the number of *Bacteroides, Bifidobacterium*, and *Clostridium*, while there was no effect on *Lactobacillus*. This could be explained by anaerobic spectrum of metronidazole. *Bacteroides, Bifidobacterium*, and *Clostridium* being obligate anaerobes are reduced by metronidazole treatment, whereas *Lactobacillus* being facultative anaerobe is not affected.

The second remarkable observation from this study was the highly significant occurrence of *Peptostreptococcus* (25/35 ALA cases, 71.4 % occurrence) and, less frequently, *Bacteroides* (5/35 ALA cases, 14.2 % occurrence) in the pus samples of ALA patients. The possible mechanisms for the presence of these bacteria in the pus samples could be intestinal bacterial overgrowth, increased permeability of mucosal barrier, and deficiency in host immune response.

Metronidazole resistance-associated genes (*nim* genes) have been associated with anaerobes including *Bacteroides* and *Peptostreptococcus* [40, 41]. We determined the presence of *nim* genes [42, 43] in all fecal and pus samples by PCR amplification with nim-specific primers. Amplicons of the sizes expected for the *nim* gene were present in both pus and fecal samples of ALA patients. However, these were not observed in *E. histolytica*-negative individuals and asymptomatic carriers. Resistance genes were present only in ALA patients because of rapid amplification of these genes in bacteria after metronidazole exposure. This was further confirmed by demonstrating these genes in healthy volunteers and IBS patients after metronidazole exposure.

In another study, real-time PCR (RT–PCR) was used for absolute quantification of gut flora in patients suffering from amoebic dysentery for 5–7 days. We also studied the presence of *nim* genes in this group of patients. We observed a significant decrease in population of *Bacteroides, Clostridium coccoides* subgroup, *Clostridium leptum* subgroup, *Lactobacillus, Campylobacter*, and *Eubacterium* in *E. histolytica*-positive samples when compared to that of healthy control samples (Fig. 3). Surprisingly, we observed a significant rise in the population of *Bifidobacterium* in amebic samples. There was no change in the population of *Ruminococcus*. This paradox can be explained by competition of *Bifidobacterium* and *Ruminococcus* for mucus as their energy source. Mucus secretion is increased in amebiasis as a result of the mechanism exerted by intestinal epithelial cells to counter the adherence of *E. histolytica* trophozoites to intestinal epithelial surface. This promotes increased colonization of *Bifidobacteria*. *Bifidobacteria* are also known to protect the gut through production of acetate. We also observed a significant increase in copy of *nim* gene in *E. histolytica*-positive samples compared to samples from healthy persons.

Such changes in bacterial population in the normal microbiota could have considerable consequences in terms of functional potential of gut flora and could result in metabolic conditions favorable for the establishment of opportunistic pathogens (e.g., *Clostridium difficile*). However, our study cannot conclude that observed changes in the gut flora are the cause or effect of the infection or the effect of dysenteric mechanism per se by the parasite. These findings have laid the platform for further research into dietary/probiotic interventions, which would have an impact on the gut flora–*Entamoeba* interaction for the benefit of the host.

Gut flora and inflammatory bowel disease

IBD is believed to result from an abnormal immune response to intestinal microbiota in genetically susceptible individuals [44]. Indirect evidence for the role of microbiota in the pathogenesis of IBD includes studies that have demonstrated evidence of mucosal T cells against gut microbiota [45] and mucosal secretion of immunoglobulin G antibodies in IBD patients [46] (Fig. 5). Recent trials in mild-to-moderate Crohn's disease (CD) have shown improvement with rifaximin [47].

Gut microbiome studies in IBD patients have demonstrated reduced diversity in the bacterial population [48],

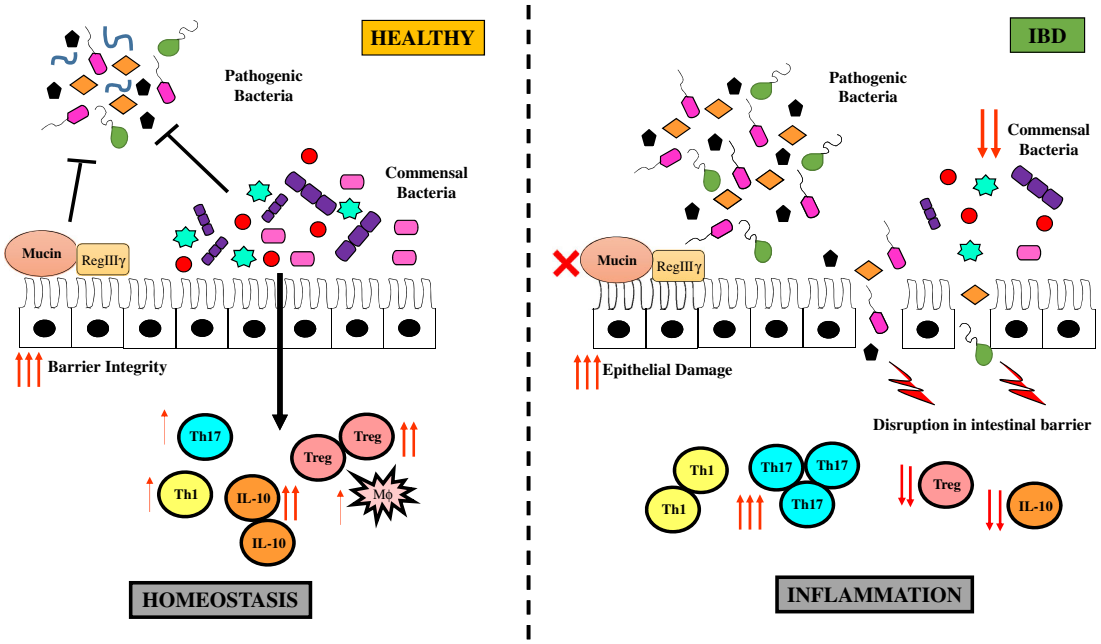

Fig. 5 Interplay of microbiome and immune system in healthy gut and in chronically inflamed gut

especially because of reduced diversity within the *Firmicutes* phylum [49–51]. Few studies have also shown an increased diversity in fungal population in patients with IBD [52, 53].

Studies from IBD patients and mouse models have shown increased population of pathogenetic bacteria including *Enterobacteriaceae*, especially *Escherichia coli* (adherent-invasive strains) [54]. These bacteria have been isolated from ileal biopsy samples in ileal CD [55] and ulcerative colitis (UC) patients [56]. Treatment with mesalamine has shown to decrease the population of these bacteria. *Fusobacterium* is another group of pathogenetic adherent-invasive bacteria, which have been found to be increased in colonic mucosa of UC patients [57, 58]. A number of protective bacterial species have been found to be decreased in IBD patients. These include *Bifidobacterium*, *Lactobacillus* [59], *Faecalibacterium* [60]. Lower levels of *Faecalibacterium prausnitzii* have been associated with a higher risk of disease recurrence after surgery in Crohn's disease patients [61].

We studied mucosa-associated bacterial flora from control individuals and IBD patients by real-time analysis using 16S rRNA-based genus-specific primers [62] (Fig. 6). There was a significant decline in the population of *Bacteroides, Lactobacillus, Ruminococcus*, and *Bifidobacterium* bacteria in both ulcerative colitis (UC) and Crohn's disease (CD) patients. Similar results have been reported in earlier studies [63–65]. The *Clostridium leptum* subgroup was reduced non-significantly in CD patients but increased sharply in UC patients, as observed in earlier studies [65–67]. The difference was more pronounced between UC and CD patients. The *C. leptum* group encompasses several butyrate-producing bacterial strains; hence, the decreases in their populations could play a role in the onset of CD. On the other hand, coccoid rods of Gram-positive *Eubacterium* and *Peptostreptococcus* bacteria were increased significantly in CD patients but not in UC patients. *Campylobacter* bacteria were significantly increased in both UC and CD patients when compared with the levels for the controls, and the levels for UC and CD patients were significantly different from each other. With the severity of the disease, the *Campylobacter* population increased significantly but reverted to normal during the remission stage. Our study also recorded increases in the populations of two subdominant inhabitants, the methanogenic bacterium *Methanobrevibacter* and sulfate-reducing bacteria (SRB) in both UC and CD patients, when compared with the levels for the controls. Therefore, there is clear delineation in concentration of bacteria between the predominating and subdominating genera under disease conditions, indicating that the subsets of bacteria participating in the pathogenesis of UC and CD are likely to be different [68].

In contrast to the mucosal studies, we found that *lactobacilli* in the fecal samples in patients with active UC are significantly increased as compared to healthy controls (unpublished data). Validation of *Lactobacillus* genus-specific probe was done by FISH-microscopy where hybridization of the probe was clearly seen with members of *Lactobacillus/Enterococcus* group. These levels of

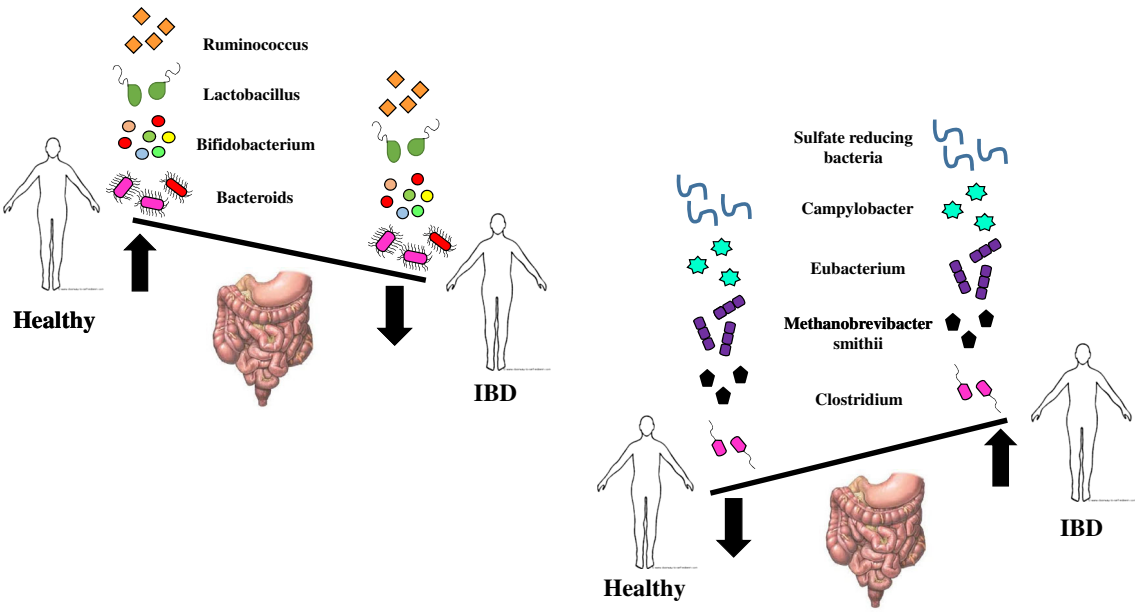

Fig. 6 Dysbiosis in IBD as compared to healthy individuals

Lactobacilli significantly reverted back to normal during remission, close to controls. Similar results have also been reported in other studies [69–71]. This was further supported by an increase in fecal lactate level (as measured by gas chromatography) in severe UC patients as compared to controls. Increased lactate level in IBD fecal samples has been detected earlier [72] and has been found to be associated with a higher risk of diarrhea and mucosal inflammation [73]. To explain the abundance of lactobacilli in fecal samples, we found significantly decreased expression of MUC9 mRNA in colonic mucosa of active UC patients as compared to controls. Therefore, increased fecal *Lactobacilli* population during active condition could be due to loss of mucin necessary for their adherence to the intestinal epithelial cell lining [74, 75]. We also found a high degree of diversity in moderate and severe category of samples [by urea PAGE (polyacrylamide gel electrophoresis) fingerprinting] as compared to controls.

In addition to differences at the phylogenetic level, there are differences in the functional composition of gut microbiota in IBD patients as compared to controls. One of the most important functions is production of short-chain fatty acids (SCFAs) by fermentation of undigested carbohydrates. These SCFAs have been depicted to regulate transepithelial transport [76], colonocyte proliferation and differentiation [77], mucosal inflammation [78, 79], intestinal motility, and barrier function [80]. Many short-chain fatty acids (SCFAs) producing bacteria are decreased in IBD patients [51]. These include *Faecalibacterium* [81, 82], *Odoribacter, Leuconostocaceae, Phascolarctobacterium,* and *Roseburia*. Other metagenomic changes in patients with IBD include increase in the functions of auxotrophic and pathobiont bacteria, which include a decrease in amino acid biosynthesis and an increase in amino acid transporter genes [51]. There is an increase in sulphate-reducing bacteria such as *Desulfovibrio* [83], increased glutathione and riboflavin metabolism [51], and increased secretion of toxins along with an increase in bacterial genes related to virulence factors [84].

We also studied the interplay between butyrate concentration and butyrate-producing bacteria in fecal samples of UC patients compared to healthy controls. Fecal samples were collected from 14 control individuals (hemorrhoid patients only) and 26 UC patients (severe $n = 12$, moderate $n = 6$, remission $n = 8$). Fluorescent in situ hybridization was employed in combination with flow cytometry to enumerate the *Clostridium* cluster population targeted by the 16S rRNA gene probe. Major butyrate-producing species within this cluster were quantified to see if any change existed in control vs. UC patients with different disease activity. This observed change was further validated by qPCR. In addition to this, gas chromatography was used to evaluate the changes in concentration of major short-chain fatty acids (SCFAs), namely acetate, *n*-butyrate, and iso-butyrate. There was a significant decrease of *Clostridium coccoides* and *Clostridium leptum* clusters in fecal samples of UC patients. Furthermore, it was observed that some butyrate-producing members of the *clostridial* cluster, like *Faecalibacterium prausnitzii* ($p = 0.0001$) and *Roseburia intestinalis* were differentially present in patients with different disease activity. In addition, this study also showed decreased concentrations of fecal SCFAs, especially of *n*-butyrate, iso-butyrate, and acetate, in the fecal

samples of UC patients. The observed decrease of predominant butyrate producers of *Clostridial* clusters correlated with the reduced SCFA levels in active UC patients. This was further confirmed by the restoration in the population of some butyrate producers with simultaneous increase in the level of SCFA in remission samples. The results of this study supported similar observations made in earlier studies [70, 85].

Therefore, alterations in the population of microbiota with respect to disease type and severity as described here may play a role as biomarkers that may help to predict disease predisposition, activity, severity, and responsiveness to therapy. One can predict the disease activity of UC by measuring the level of these species and concentration of SCFAs in stool samples and this method can be developed as a non-invasive marker for disease activity.

Therapeutic applications of microbiota in IBD

Therapeutics with microbiota in IBD include the use of probiotics that are defined as "live microorganisms, which when administered in adequate amounts confer a health benefit to the host [86]" and fecal microbiota transplantation. The beneficial effects on health by replacement of healthy bacterial flora are shown in Fig. 7.

There are specific requirements for probiotics before clinical use. They should be of human origin, genetically stable, and should be resistant to the acid, bile, and digestive enzymes in the GI tract. They should also have a safety record in human intervention trials. However, data on the use of probiotics are limited, and a strong consensus cannot be drawn from the current literature. In a recent meta-analysis [87] (which included only full text papers in English), there were 41 studies that were categorized on the basis of disease type and severity. There was marginal, non-statistically significant benefit with *Bifidobacterium* fermented milk versus placebo [88, 89] [RR: 2.7 (95 % CI 0.47–15.33)] and VSL#3 versus placebo [90–92] [RR: 1.88 (95 % CI 0.96–3.67)] in inducing remission in active UC. There was no benefit with *E. coli* Nissle 1917 versus standard treatment [93, 94] for preventing relapses in inactive UC, VSL#3 versus placebo for preventing relapses in inactive UC [95]/ileo-anal pouch anastomosis [96–99]; preventing endoscopic recurrences in inactive CD with *Lactobacillus rhamnosus GG* [100, 101] versus placebo and for preventing endoscopic recurrences in inactive CD with *Lactobacillus johnsonii* versus placebo [102]. The conclusions drawn from this meta-analysis were that the evidence from the current trials is weak and further well-designed randomized controlled trials are required before probiotics can be recommended for treatment of IBD. In addition, probiotics have shown some evidence in induction of remission in cases of microscopic colitis [103].

Fecal microbiota transplantation (FMT) gained popularity with its excellent treatment efficacy in difficult-to-treat patients with *C. difficile infection* [104, 105]. After 2013, data is emerging for its role in treating patients with IBD. A recent systemic review and meta-analysis of cohort

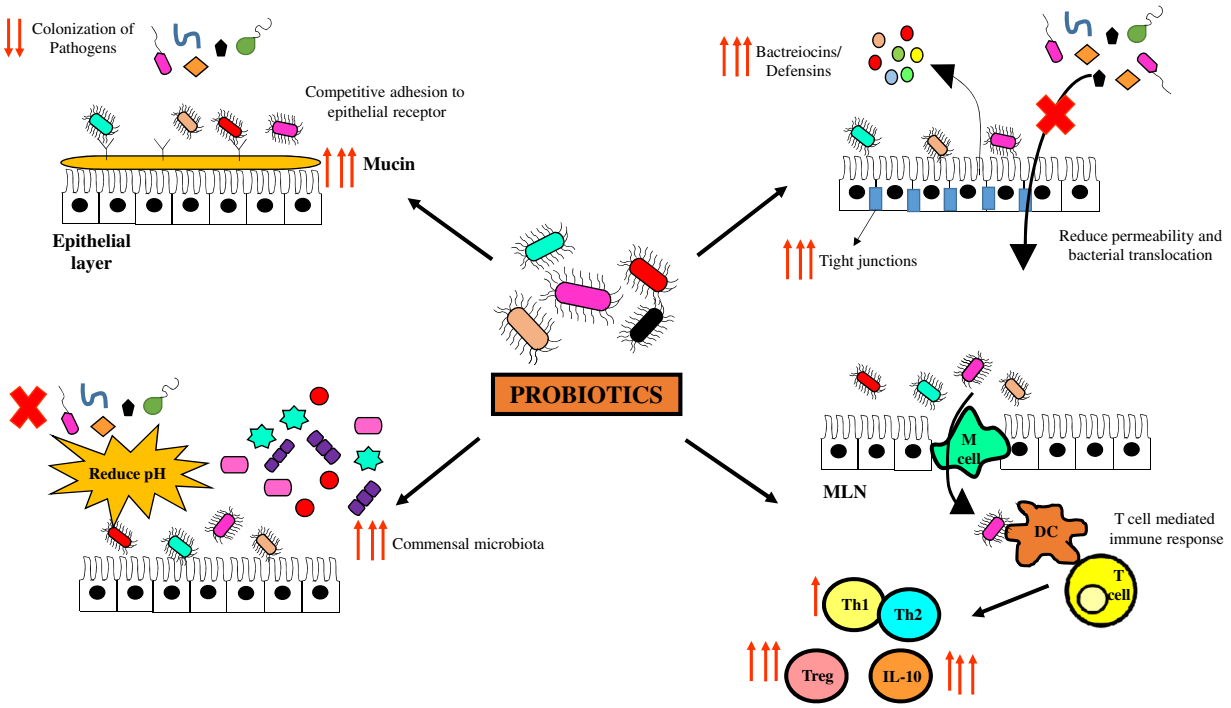

Fig. 7 Beneficial effects of probiotics on human gut

studies clarified the role of FMT in IBD [106]. This meta-analysis included 18 studies (122 patients: 79 UC, 39 CD, four IBD unclassified). The overall remission rate was 45 % with FMT. However, in a meta-analysis of cohort studies, the pooled proportion of patients who achieved remission was 36.2 %. In the subgroup analyses, the proportion of UC patients who achieved remission was only 22 % [107–111], and the proportion of CD patients who achieved clinical remission was 60.5 % [112–115]. Most of the donors were first-degree relatives of these patients. FMT delivery methods were enemas, colonoscopic, nasogastric/nasojejunal, and gastroscopic installation. The FMT frequency was variable among the studies. FMT was well tolerated and no study reported any serious adverse events. Six studies also did microbiota analysis. There was a significant reduction in Proteobacteria and an increase in *Bacteroidetes* after FMT [110]. At the metagenomic level, there was an increase in butyrate-producing groups in responders as compared to non-responders. However, the data on FMT is still in its infancy. As per the current literature, it is a safe but variably efficacious treatment for IBD.

Conclusions

We studied the gut microbiome (both fecal and mucosal) in a varied spectrum of intestinal diseases ranging from acute and chronic infections to chronic autoimmune diseases like inflammatory bowel disease in a unique population which is endemic for infectious diseases and has an increasing burden of autoimmune diseases. We found the microbiome perturbations to be generally similar in infectious and autoimmune diseases. The population of useful bacteria such as lactobacilli was decreased in both amebiasis and ulcerative colitis while the population of pathogenetic bacteria were increased in both amebiasis and IBD. Although the microbiome would vary at the phylogenetic level, the alteration in functional composition was essentially similar in these diseases. Therefore the presence of inflammation would be the major engine for microbiome alterations in these diseases. These studies provide the platform for investigating microbiome diversity perturbations in diseases with varying etiology as well as a roadmap for therapeutic microbiome manipulation in a population which is unique as it displays a high prevalence of both enteric infections as well as gut autoimmune diseases.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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