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The Gut Microbiota in Ulcerative Colitis-Mini review

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ABSTRACT :
Microbiota in the intestines and the host interact with each other, affecting the host's health and, in turn, the arrangement of gut microbiota. The two important characteristics in this regard are a decrease in beneficial bacteria and an increase in harmful bacteria. In the normal health state, these life forms are in a symbiotic relationship with the host where they can provide some biological functions not executed by the host. Vitamin K biosynthesis is a well-known example of this. On the other hand, in a disease state, these microbiota communities become disturbed where beneficial members are lost in favour of some pathological forms which may increase the pathological process.. Changes in the makeup and quantity of the gut microbiome have been shown to be valuable as diagnostic markers. The gut microbiota plays an essential role in Ulcerative collitis. In this review, we reviewed some of these microbiota changes in different gastrointestinal diseases.

Keywords: Gut microbiota, Inflammatory bowel disease, Crohn's disease, ulcerative colitis, biomarkers

Introduction:

Ulcerative colitis (UC), a nonspecific intestinal inflammatory disease, is characterized by recurrent abdominal pain, diarrhea, bloody or purulent stool, and weight loss (1). Inflammation and mucosal damage in the colon, which generally start in the rectum and continuously extend to proximal segments of the colon, are its main pathological manifestations (2). Due to its prolonged disease duration and difficult therapy, patients with UC may need lifelong treatment (3). On account of the long-term and chronic intestinal

inflammatory stimulation, the incidence of UC-associated colorectal cancer, as well as mortality rate, in patients is increasing gradually (4).

Recurrent flare-ups of inflammation characterise ulcerative colitis. Although inflammatory involvement is limited to the mucosal layer, it is most typically observed in the rectum. It demonstrates continuous engagement in the colon with no gaps in between. It is typically characterised by bloody diarrhoea, with no involvement of the small intestine. According to the severity of the symptoms, UC is classified as mild, moderate, severe, or more severe (fulminant). In the mild grouping, involvement is usually limited to the rectum, whereas in the moderate subgroup, involvement extends up to the splenic flexure. In severe and fulminant subtypes, colonic involvement is widespread. Unlike UC, Crohn's disease can affect any part of the GI tract, but it most commonly affects the terminal ileum (5)

Under normal circumstances, gut microbiota exerts many physiological functions. This involves augmenting the host metabolism through the expression of many metabolism-related genes lacking in the human genome **[6]**. In this regard, most of the energy consumed by the colonic epithelial cells is provided by the gut microbiota as short chain fatty acids (SCFA) through digestion of unabsorbed carbohydrate **[7]**. Moreover, gut microbiota has a recognized role in the immune system regulation and programming **[8, 9]**. A traditional role that the gut microbiota has long been known for is the protection against invasion and colonization by different pathogens **[10]**

In this article, we reviewed gut microbiota disturbance patterns encountered in some of the most common GI diseases like ulcerative colitis.

Gut microbiota in ulcerative colitis:

Both experimental and human studies showed gut microbiome disruption. In human studies, "diversion colitis" may be an early indicator of the importance of the gut microbiome in maintaining healthy gut homeostasis, and its absence or disruption may be responsible for colitis [11]. Furthermore, the historical use of probiotics for the treatment of UC, albeit with no substantial impact, was another indication of the importance of gut microbiota disruption in the pathogenesis of UC[12].

In UC patients, there is a continuous depletion of the beneficial short chain fatty acid (SCFA) generating species *Fecalibacterium Prausnitzii* in favour of the potentially dangerous Enterobacteriaceae family (Escherichia/ Shigella). These pathogenic bacterial members can trigger proinflammatory responses, accelerating the development and progression of UC [15]. This could be accomplished through molecular mimicry or bacterial translocation, resulting in immune system activation[16].Some aspects that predispose to IBD development and flares can be explained by gut flora. One example is the influence of dietary iron, which causes an increase in some iron-dependent species such as the pathogens *E. coli* and *Klebsiella*, which can then stimulate an inflammatory response with IBD flare[17].

Patients with UC have gut dysbiosis, as evidenced by a large drop in health-associated species such as *Roseburia* and *Akkermansia muciniphila*[18], as well as an increase in possible pathogens such as Fusobacterium, Helicobacter, *E. coli*, and *C. difficile* [19-21]. *F.Prausnitzii*, on the other hand, appears to have a protective effect against colitis, as demonstrated in a cohort of 116 individuals with UC, where patients and their relatives had

reduced abundances of *F. Prausnitzii* compared to healthy controls. Furthermore, a decrease in *F. Prausnitzii* was linked to a higher risk of relapse and more frequent relapses during the first year after remission induction[22].Similarly, a small Italian cohort of UC patients demonstrated a substantial drop in *Bifidobacterium bifidum* species (Bifidobacterium genus) in active disease compared to both healthy controls and those in remission[23].

Interestingly, infants born to IBD mothers had similar gut dysbiosis, with an increase in the Gamma proteobacteria class and a significant drop in the *Bifido* bacterium genus, which might be attributed to maternal IBD (after controlling for other factors) [24]. This study suggests that gut bacteria may play a role in the familial aggregation of IBD patients. Long-term research are needed, however, to support or refute this idea.
Patients with UC had reduced abundances of the SCFA producers *Roseburia, Phascolarcto* bacterium, and *Leuconostocaceae* in a cohort of 228 participants (including 75 UC patients) from the prospective PRISM and OSCCAR trials. Furthermore, patients with pancolitis demonstrated Odoribacter depletion [25]. Other alterations in gut microbiota observed in this study (including a decrease in *Anaerostipes, Collinsella, Butyricicoccus, Subdoligranulum, Dorea,* and an increase in enterococcus) were attributed to age, drugs, smoking, and sample site. As a result, aside from disease activity and extent, a variety of variables may have a role in the dysbiosis observed in IBD (UC & CD) patients, with varying effect sizes. Age, treatment status (including antibiotics and immunosuppressants), and environmental factors such as smoking are examples of these. This was confirmed in a recent multi-center longitudinal study on IBD patients (303 CD patients, 228 UC patients, and 161 controls), where geographical location, diet, history of resection surgery, and alcohol consumption all played a role in the differences in gut microbiota between IBD patients and healthy controls [26].
A recent investigation on a Polish cohort of moderate to severe UC patients found higher abundances of *Actinobacteria* and *Proteobacteria*, as well as lower abundances of *Bacteroidetes* and Verrucomicrobia, compared to healthy controls[27].
A cross-sectional research of an Italian population with IBD found that IBD patients had greater *Firmicutes*, *Proteobacteria*, *Verrucomicrobia*, and *Fusobacteria* phyla and lower *Fusobacteria* and *Cyanobacteria* phyla. In addition, UC patients demonstrated a substantial increase in *actinobacteria* as compared to controls. Patients with CD had significantly reduced levels of *Bacteroides, Fecalibacterium Prausnitzii*, *Prevotella*, *flavobacterium*, and *Oscillospira* at a lower phylogenetic level. Furthermore, these patients had elevated levels of *Escherichia, Veillonella, streptococcus, and Ruminococcus*. Despite having similar dysbiosis, individuals with UC had an opposing shift of *F. Prausnitzii* that was higher than controls but did not achieve significance [28].

In addition to the dysbiosis commonly seen in UC patients, the physiological interactions between gut microbiota and gene expression were found to be significantly disrupted in UC, with fewer detected correlations between mucosal transcriptional profiles and gut microbiota in UC patients and their unaffected discordant twins compared to healthy controls. In UC, the transcriptional profile associated to oxidative stress was increased[29].

While primary sclerosing cholangitis (PSC) is strongly associated with UC[30], and while they share common features in the gut microbiota patterns, PSC has been linked to an increase in some bacterial species that are not associated with UC, such as *Rothia*, *streptococcus*, *enterococcus*, *Clostridium*, *Veillonella*, and *Hemophilus*. Some organisms, such *as Fusobacteriaceae*, were more prevalent in UC than in PSC-IBD[18].

Another cross-sectional study with PSC (with or without UC) and UC-only patients yielded similar results. Although all patient groups showed lower microbiota diversity when compared to healthy controls, patients with PSC had a distinct microbiota profile that allowed them to be distinguished from both healthy controls and patients with UC who did not have hepatic illness. *Veillonella* was found in much greater abundance in PSC patients. Surprisingly, the presence of UC had no effect on the gut microbiota pattern seen in PSC patients[31].

Furthermore, experimental research could shed light on the involvement of gut bacteria in the development of UC. Even with genetic changes known to produce spontaneous colitis, such as IL-10 deficiency, germ free mice (GF) did not develop colitis [32, 33].

Furthermore, monocolonization of IL-2 deficient mice (colitis mouse model) with *E. coli* was shown to promote colitis, whereas monocolonization with *Bacteroides vulgatus* was shown to protect against the disease, both actions were shown to be through an effect on lamina propria dendritic cell functions, leading to either proinflammatory or immunomodulatory actions [34].

Furthermore, when given as enemas into mice models, *Fusobacterium* (derived from UC patients) culture supernatant produced a state comparable to ulcerative colitis, including crypt abscesses and ulcers[35].

CONCLUSION:

The above-mentioned changes in gut microbiota in various gastrointestinal illnesses provide insight into the potential function of gut microbiota in the development of ulcerative colitis. Extensive studies linking the gut microbiota of patients with UC to that of healthy participants can provide valuable insights into the role of gut microbiota in UC. Ulcerative colitis is a complex inflammatory bowel disease, and the gut microbiota has been associated in its pathogenesis and progression.

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