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MICROBIAL BIOSYSTEMS
INTERNATIONAL SCIENTIFIC JOURNAL OF MICROBIAL BIOLOGY

Microbiota and its relationship with Inflammatory Bowel Diseases: An overview

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ABSTRACT

The human body's microbiome is essential for immunity and fighting off illness. Many bacteria in the intestinal system are beneficial, playing roles in immunological control and intestinal homeostasis. Understanding the contributions of "good bacteria" to these processes is, therefore, crucial. Advanced research into the microbiota and microbiotas is providing an increasingly deep understanding of the composition of the human microbiota, relationship between the microbiota and genetic susceptibility to disease, and the role of microorganisms in immune-related diseases. This review article discusses the effect of microbiota on patients with inflammatory bowel disease (IBD) to understand the role that their microbiota may play in efforts to treat both types of the disease, including ulcerative colitis and Crohn's disease. Clinical studies demonstrate that specific probiotic strains such as *Lactobacillus rhamnosus* GG and *Bifidobacterium animalis* subspecies *lactis* aid can inhibit pathogenic organisms (both bacterial and viral). Overall, this review article may assist to promote public health and the prevention of future illness since dysbiosis, which is defined as a loss of diversity in the microbiota makeup of an individual, can affect acquired immunity. This review of information also emphasizes need for further research on microbiota and its association with digestive and related diseases.

Introduction

The genomic makeup of the organisms (microbiota) that reside in the human body is referred to as the human microbiota, and the collection of organisms living in and interacting with the human body is referred to as the human microbiota. Numerous anatomical body locations, including the skin, mucosa, gastrointestinal system, respiratory tract, urogenital tract, and mammary glands, are colonized by microorganisms. Thus, in healthy individuals, healthy bacterial communities are found in the oral cavity, oesophagus, stomach, small intestine, and colon. The species isolated from the oral cavity include *Streptococcus*, *Prevotella*, *Porphyromonas*, and *Fusobacterium* strains, and the stomach accommodates *Streptococcus*, *Lactobacillus*, *Staphylococcus*, and

Peptostreptococcus, with 400 to 1,000 species commonly found in the small and large intestine. Most of these species are anaerobes; indeed, two to three times more facultative anaerobes are found in these locations than aerobes. The most common species belong to the phyla Firmicutes and Bacteroidetes, with fewer *Proteobacteria*, *Fusobacteria*, *Cyanobacteria*, *Verrucomicrobia*, and *Actinobacteria* strains (Marsh & Percival, 2006; Flint et al., 2010; Rosen et al., 2014; Lu et al., 2015; Ren et al., 2017; Corfield, 2018).

In this review article has discussed the types and composition of bacteria in the intestinal microbiota, benefits of the microbiota, their genetic susceptibility, and the relationship between these microbiota and human diseases. Such as microbiological causes of Inflammatory

bowel disease (IBD), including Ulcerative colitis (UC), the Risk factors for UC, Crohn's disease (CD), the Symptoms of CD and the Risk factors for CD.

1. Types of bacteria in the intestinal microbiota

The gut microbiota includes beneficial bacteria, conditional pathogenic bacteria, and pathogenic bacteria. In healthy people, beneficial bacteria are dominant in the intestinal tract, where they help to maintain intestinal homeostasis and immune regulation. An increase in the proportion of harmful bacteria in the gut, or, an imbalance between beneficial and harmful bacteria, results in disease. The metabolism of these organisms under homeostasis produces numerous substances that are beneficial for the host, whereas unbalanced conditions affect the growth and health of the host (Zhang et al., 2016; McCabe & Parameswaran, 2018; Wang et al., 2018).

2. Composition of the human microbiota

Humans are exposed to microbiota and chemicals that it releases intra-arterially, and this exposure increases significantly after birth. The gut of a new-born can become colonized by any environmental microbe that satisfies the physicochemical conditions of that environment, in particular, by organisms in the mother's vaginal fluids, skin microbiota, and/or breastmilk (Dominguez-Bello et al., 2010). Vaginal birth and breastfeeding thus promote the proliferation of beneficial microbes in new-born (Milani et al., 2017). Accordingly, for babies delivered through cesarean section, exposure to the mother's vaginal fluid can partially restore the microbiota (Dominguez-Bello et al., 2016). The sialylated milk oligosaccharides in breastmilk can promote the growth and development of infants by encouraging the spread of beneficial microflora (Charbonneau et al., 2016), while the synergistic interplay of breastfeeding and saliva in the infant's mouth improves innate immunity by modifying the oral microbiota (Sweeney et al., 2018).

3. Benefits of the microbiota

The microbiota at adulthood appears to be stable throughout most of an individual's life (Patel et al., 2016). In fact, individuals' food patterns affect gene expression, metabolism, and intestinal development in their offspring by influencing colonization by intestinal flora (Sonnenburg & Sonnenburg, 2014). The core microbiota of the elderly participants in one study, however, differed from that of previously studied younger adults, being characterized by more *Bacteroides* spp. and unique patterns of *Clostridium* group abundance (Claesson et al., 2011). Therefore, as individuals grow, their microbial flora is constantly changing in ways that are important for the adaptation of certain physiological states to changes in the environment

and in the host (Goulart et al., 2020).The wide range of microbial species found in the human gut facilitates digestion, food absorption, and defense against harmful microorganisms (Khaneghah et al., 2020). Several of these species maintain the mucosal barrier that shields the cells lining the intestinal tract from stomach acids and digestive enzymes. Gut microorganisms also interact with the mucosal immune system in ways that can facilitate the early diagnosis and treatment of illnesses (Claus et al., 2016; Liu et al., 2020) and promote the synthesis of enzymes, including those that expedite the conversion of carbohydrates into metabolites (Cani et al., 2019).

In addition, various bacteria in the stomach create propionate, acetate, and butyrate enzymes that help epithelial cells to differentiate, express certain genes, and proliferate (Zaiss et al., 2019). The microbiota of the digestive system, therefore, contributes significantly to pathogenesis, immunity, digestion, and cell growth (Al-Judaibi, 2021).

4. Microbiota and genetic susceptibility

The genetic susceptibility of individuals to various conditions such as antibiotics is influenced by their surroundings as well as by the relationship between their intestinal microbiota and their immune systems (Caviglia et al., 2019; Khan et al., 2019). Environmental variables may play a significant role in causing or determining the progress of disease, as variations in the epidemiology of IBD over time and across geographic regions demonstrate (Ribaldone et al., 2019). Urbanization has been linked to dietary modifications, the use of antibiotics, distinct sanitary conditions, exposure to distinct microbes, and pollution, all of which are potential environmental risk factors for IBD. In large part, dysbiosis appears to be a side effect of the Westernization of lifestyle. Thus, for example, patients with Crohn's disease have less microbial diversity than individuals without the disease (Mirsepasi-Lauridsen et al., 2018; Ribaldone et al., 2019).

5. Relationship of intestinal microbiota and disease

The relationship between the microbiota and certain disease states has been recognized for more than a century. Previous research has directly linked dysbiotic gut flora to, in addition to IBD, changes in the immune environment as well as potentially life-threatening conditions ranging from cancer and cardiovascular disease to difficult-to-treat infections with antibiotic-resistant bacteria (Morgan & Huttenhower, 2012 ; Whiteside et al., 2015; Ogunrinola et al., 2020). The advent of next-generation sequencing tools over the past decade has greatly increased the understanding of the human microbiota, including the association of more and more illnesses with changes in the microbiota and its

metabolome. Notably, the widespread use of antibiotics has coincided with an increase in the prevalence of autoimmune disorders such as IBD, type 1 diabetes, multiple sclerosis, and systemic lupus erythematosus (Bach, 2002 ; Gilbert *et al*., 2018; Vangoitsenhoven & Cresci, 2020).

6. Microbiological causes of IBD
Inflammatory bowel disease (IBD), is the general term for a chronic inflammatory disorder of the gut with intestinal and systemic abnormalities, including Crohn's disease (CD) and ulcerative colitis (UC). In the United States, the incidence of CD ranges from 6 to 8 per 100,000 people (Herrinton et al., 2008) and the incidence of UC ranges from 9 to 12 cases per 100,000 people (Kappelman et al., 2007; Shivashankar et al., 2017).

According to Neovius et al., (2013), many IBD patients experience crippling life-long physical symptoms, including urgent diarrhea, rectal bleeding, vomiting, anorexia, and lethargy. As a result, they frequently suffer from poor psychosocial well-being and encounter difficulties with respect to academic performance, employment, relationships, and sexual health. Unsurprisingly, the financial costs of IBD are significant (Solberg et al., 2007; Everhart & Ruhl, 2009).

7. Approaches to the study of the microbiological causes of IBD
The theories and hypotheses developed by researchers tend to attribute IBD to persistent pathogens, excessive bacterial translocation, and dysbiosis. Firstly, hypothesis suggests a leading role of persistent enteric pathogens as adhesion-invasive *Escherichia coli*, *Clostridium difficile*, and *Mycobacterium avium* subspecies *paratuberculosis* (AIEC) (De Hertogh et al., 2008; Kalischuk & Buret, 2010. Secondly, theory explains that disease occurs when an unusually high number of intestinal bacteria cross the intestinal barrier, thus the dysbiosis theory associates the disease with change in the ratio of "helpful" to "detrimental" commensal bacteria. And thirdly, theory explains that mutually exclusive is not necessary; for instance, *Mycobacterium avium* subspecies *paratuberculosis* (AIEC) is both a harmful commensal bacterium and a chronic pathogen (Liu, et al., 2021).

7-1. Ulcerative colitis (UC)
The incidence of UC has been increasing worldwide, and it now affects nearly 1 million people, including close to 1 million each in the United States and Europe (Rubin et al., 2019). UC is a long-lasting, immune-mediated inflammatory disorder of the large intestine that commonly involves inflammation of the rectum but can also affect other sections of the colon. One study reported that fewer than 5% of adult UC patients had no rectal involvement at diagnosis while up to one-third of pediatric-onset patients may present in this way (Glickman & Odze, 2008). Initial signs of UC include bleeding, urgency, and tenesmus (a sense of pressure), which are signs of an inflamed rectum. The illness may manifest at any time and at any age, but the age distribution of onset peaks between 15 and 30 years.

The pattern of disease activity is usually described as relapsing and remitting, with symptoms of active disease alternating with periods of clinical quiescence, or remission (Fumery et al., 2018). Some UC patients experience persistent disease activity after diagnosis despite medical therapy, and a small number present with rapid-onset, progressive "fulminant disease" (Fumery et al., 2018). While UC has a low rate of mortality, it produces severe morbidity (Bernstein et al., 2013; Jess et al., 2013). As mentioned, patients with active disease often experience barriers to social interactions and job advancement and concomitant psychiatric problems such as anxiety and depression (Regueiro et al., 2017). Long-standing UC is also associated with an increased risk of dysplasia and colorectal cancer presumably caused by the persistent uncontrolled inflammation (Rutter et al., 2004; Herrinton et al., 2012; Rubin et al., 2013; Colman & Rubin, 2016; Rubin et al., 2019).

7-2. Crohn's disease (CD)
Chronic gut inflammation is a hallmark of the complicated immune-mediated condition known as CD. Periods of remission from the illness punctuated by flare-ups—bouts of increased inflammatory activity—are common. Inflammation is a product of the complex relationship between genetic predisposition and environmental conditions. The symptoms, location, and behavior of CD vary depending on patients' age at onset and level of inflammation in the gastrointestinal tract. Because there is no one universal definition for the condition, several investigative methods are frequently required to confirm a CD diagnosis (Feakins, 2013). The most widely accepted framework for making a diagnosis date back nearly 30 years. Factors include an appropriate clinical history and examination, ileocolonoscopic, small bowel imaging, blood tests and histology. Mucosal biopsies from endoscopic procedures or surgical resection specimens serve to indicate localized or patchy inflammation as opposed to widespread inflammation. Skip lesions, granulomatous inflammation, ileal involvement, and a propensity for inflammation, especially in the proximal colon, are also symptomatic of CD (Lamb et al., 2019). A recent study identified dysbiosis with reduced variety as the defining feature of the disease (Halfvarson et al., 2017). Though the significant role of the microbiota in disease pathogenesis

is well-known (Gevers et al., 2014; Schaubeck et al., 2016), the particular bacterial taxa responsible for inducing inflammation and the underlying mechanisms have not yet been identified (Björkqvist et al., 2019; Zhulina et al., 2013).

Numerous studies have shown a correlation between the prevalence of CD and decreased numbers of Gram-positive bacteria and possible compensatory increases in Gram-negative bacteria (Huttenhowere et al., 2014; Salamon et al., 2020) identified lipopolysaccharide, a component of the Gram-negative cell wall, as the probable key factor in the development of the disease through effects on the immune system and by inducing inflammation (Marchesi et al., 2016). Additionally, as discussed, researchers such as (Bitton et al., 2016) have found that the effects of CD on patients' physical, emotional, and social well-being result in a significantly lower health-related quality of life (HRQoL) compared with the general population (Floyd et al., 2015 and Panaccione et al., 2019).

More than half of CD patients require hospitalization within five years of diagnosis and as many as one-third within the first year (Golovics et al., 2015). In addition to a significantly higher risk of dying from digestive diseases than those without CD, individuals with CD also have a significantly higher chance of dying from any cause (Bitton et al., 2016).

7-3. Symptoms of CD

Some individuals experience symptoms for years before being diagnosed with CD because the location and severity of the disease render the symptoms subtle and nonspecific (Danese et al., 2015). The two most common, as mentioned, are diarrhea and stomach pain, and the indicia also include persistent fistulas and other perianal abnormalities, anemia, fever, anorexia, and exhaustion ulcers or fissures (Gomollón et al., 2017; Giulia et al., 2020) The lack of bowel movements resulting from bowel blockage in people with structuring disease can cause hyperactive bowel noises, nausea, and vomiting, and a penetrating form of the disease may manifest as fistulas or abscesses, which may cause patients to experience systemic symptoms such as fever and chills and other symptoms depending on where in the body the disease is located (Peyrin-Biroulet et al., 2012; Ott & Schölmerich, 2013).

7-4. Causes of CD and UC

The aetiology of IBD is complex in that the gut microbiota, host genetics, and environmental exposure factor into its pathogenesis (Xavier & Podolsky, 2007; Garrett et al., 2010). The human gut is home to trillions of bacteria that significantly affect health, playing a role in processes ranging from food digestion to the synthesis of

vitamins. Some individuals interact with the microorganisms that inhabit them more favourably than others. Sometimes, the body's reaction to its own microorganisms is negative, triggering an excessive immune response and inflammation that can result in discomfort, diarrhoea, and IBD (whether CD or UC). Individuals with IBD experience various symptoms and respond to treatment in distinct ways. Several factors, including genetics, the status of the immune system, and gut flora, may contribute to the development of IBD. Numerous genetic variants have been identified that are associated with increased risk of developing the disease, which, thus, cannot be traced back to a single mutation, while individuals who have other genetic predispositions may remain asymptomatic. Certain immune cells, such as the white blood cells known as Th17 cells, are found in large quantities in symptomatic individuals. Additionally, compared with those who have a healthy gut, IBD sufferers may harbour distinct bacterial species, such as *Bacteroides*. The relationship between the immune response, the kinds of bacteria that exist in the gut, and the specific genes involved remain poorly understood (Lavoie et al., 2019).

7-5. Risk factors for CD

Patients with colonic involvement are more likely to develop colorectal cancer than those without, with the risk factors including the intensity of continuous colonic inflammation, the length of the illness, the degree of involvement, the presence of primary sclerosing cholangitis, and family history of the disease For individuals with CD, the relative risk of small bowel adenocarcinoma is significantly increased (at least 18-fold), though the absolute risk is still low, approximately 0.3 instances per 1,000 patient-years (Laukoetter et al., 2011). The cause of the elevated risk appears to be, again, persistent chronic inflammation (Lichtenstein et al., 2018).

Conclusions

Studies on Microbiota have extensively demonstrated that some microorganisms in the human body lead to diseases while others enhance digestion, immunity, and metabolic activities. Organisms colonize individuals at birth and remain with them throughout their lives. The microbiotas of individuals differ and change with age. Some microorganisms collaborate with the immune system and can aid in the early diagnosis and treatment of disease.

Such variables as dietary modifications, antibiotic use, individuals' health status, and pollution are considered potential environmental risk factors for IBD and play roles in the progress of the disease. IBD is chronic and relapsing, and the mechanisms behind it remain uncertain. Additional research into both types of IBD, UC and CD,

is needed to clarify the causes of the disease and the manner in which it progresses and identify effective prevention, diagnosis, and treatment strategies.

Acknowledgment

Authors like to thank the Saudi Digital Library (SDL) for access to the publications for free.

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