International Journal of Medical Science and Research
www.medicaljournals.in
Online ISSN: 2664-8768, Print ISSN: 2664-875X
Received: 05-08-2022, Accepted: 21-08-2022, Published: 07-09-2022
Volume 4, Issue 2, 2022, Page No. 51-54

A short review on dysbiosis and human gut health

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Abstract
There is mounting evidence that the development of both intestinal and extra-intestinal illnesses is influenced by gut microbiota dysbiosis. Coeliac disease, irritable bowel syndrome (IBS), and inflammatory bowel disease are intestinal illnesses. Other problems include obesity, asthma, allergies, metabolic syndrome, cardiovascular disease, and metabolic syndrome. The microbiota serves as a defence against infections, drives vital metabolic processes, and controls inflammation by igniting the immune system. Dysbiosis, a microbial imbalance in the gut, has been linked to serious human illnesses such inflammatory disorders. The current review outlines what is known about the gut microbiota in a healthy setting and looks at intestinal dysbiosis in inflammatory bowel disease (IBD) patients, the condition that has been most commonly linked to altered gut microbiota composition.

Keywords: dysbiosis, gut microflora, human digestive health, inflammatory bowel disease, metabolic syndromes

Introduction

There are billions of microorganisms in the human gut microbiota, the majority of which are non-pathogenic bacteria and viruses (Savage, 1977; Reyes *et al.*, 2010) [33, 26]. The immune system and the host's defences work together to guard against pathogen invasion and colonisation. In addition, it serves as a source of vital vitamins and minerals and facilitates the metabolic process through which food is converted into energy and nutrients including short-chain fatty acids (SCFA) and amino acids.

In the end, the host relies on its gut microbiota for a variety of essential processes, and as a result, the intestinal microbiota may support health. The precise influence of the gut microbiota on human health and its role in human disease, however, is difficult to pinpoint. Exposure to a variety of environmental variables, including as nutrition, chemicals, medicines, and viruses, can change the microbiota. Foodborne viral pathogens can alter local and systemic inflammation, changing the composition of the microbiota and barrier function, as a mechanism for developing autoimmunity, as shown in type 1 diabetes and T-cell-mediated destruction of insulin-producing pancreatic b-cells. Of these, enteric pathogens have the greatest potential to cause microbial dysbiosis as seen in experimental animal models (Kamada *et al.*, 2013; Tanoue *et al.*, 2010; Wen *et al.*, 2008) [15, 37, 41].

Dysbiosis

Dysbiosis is a term used to describe a microbial ecosystem in which bacteria cannot coexist and the "good" bacteria are unable to adequately regulate the "bad" bacteria. Currently, the autoimmune and auto-inflammatory illnesses, such as allergies, obesity, and inflammatory bowel disease, have been related with dysbiosis. However, the exact cause of dysbiosis is still unknown. Every day, more illnesses are discovered that are connected to the gut microbiota, and most of them have complicated pathophysiology and consequences. A recent study found that the formation of many tiny ovarian cysts, hyper-androgenism (acne, hirsutism), and irregular menstruation are all caused by the dysbiosis of the gut microbiota (DOGMA) (Tremellen and Pearce, 2012) [39].

The DOGMA may enhance the permeability of the gut mucosa, which would allow more lipopolysaccharide (LPS) to enter the bloodstream. Following immune system activation, blood insulin levels rise due to insulin receptor dysfunction, which in turn causes an increase in androgen production from the ovary, impairing the formation of healthy follicles (Qin *et al.*, 2012) [23]. Additionally, a mild degree of gut microbial dysbiosis was discovered even in patients with type 2 diabetes. This included a decline in the number of butyrate-producing bacteria, an increase in opportunistic pathogens, and an expansion of the microbial functions granting sulphate reduction and oxidative stress resistance (Qin *et al.*, 2012) [24].

Dysbiosis and GI-tract-related disorders

1. Inflammatory bowel disease

The most common types of inflammatory bowel disease (IBD), which are characterised by chronic recurrent inflammation affecting the intestinal mucosa, are Crohn's disease (CD) and ulcerative colitis (UC). There is growing evidence that gut microbial dysbiosis has a role in the development of IBD, even if the causes of both disorders are unclear (Baumgart and Carding, 2007) [3]. Overall, patients show a decline in the number of microorganisms in their intestines as well as functional diversity and stability of their microbiota, with reductions in certain Firmicutes and concurrent increases in Bacteroidetes and facultative anaerobes such Enterobacteriaceae (Hansen *et al.*, 2010) [11]. Significant variations between CD and UC patients' microbiome have also been observed (Frank *et al.*, 2007; Sokol *et al.*, 2008) [9, 10, 35, 18]. Faecalibacterium prausnitzii abundance changes have been linked to a longer duration of illness remission in CD, where the primary dysbiosis has been described to be connected with five bacterial species (Sokol *et al.*, 2008; Joossens *et al.*, 2011) [35, 18, 14], with this bacterium having a healing impact in colitis-related animal mice (Miquel *et al.*, 2013) [19]. On the other hand, adherent-invasive E. coli and Mycobacterium paratuberculosis have been connected to CD pathogenesis, although a direct link has not yet been shown (Darfeuille *et al.*, 2004; Rosenfeld and Bressler, 2010) [7, 29].

Tewari (2019) [42] reported that intestinal dysbiosis may have a role in the aetiology of inflammatory bowel disease (IBD), which includes Crohn's disease (CD) and ulcerative colitis, according to a developing mainstream theory (UC).

IBD are immune-mediated conditions that result from a breakdown of the healthy interaction between the commensal microbiota and the mucosal immune system (Podolsky, 1997; Sartor, 1997) [22, 32]. This results in the deregulation of the innate and adaptive immunity, the formation of abnormal reactivity against intraluminal antigens, and consequent tissue harm (Cho, 2008; Lees *et al.*, 2011) [6, 17]. Patients with IBD may lose their tolerance to some of the local microbiota for a variety of reasons, such as hereditary predisposition (Rioux *et al.*, 2007) [27], defects in mucosal barrier function (Rakoff *et al.*, 2004) [25] and imbalance in the composition of the gut microbiota (Tamboli *et al.*, 2004) [36]. In CD, over 71 susceptibility loci have been identified (Walker *et al.*, 2011; Rivas *et al.*, 2011; Inohara *et al.*, 2003) [40, 28, 13]. Numerous gene products have been discovered that play a role in the processing and identification of microbial antigens at the mucosal surface. The polymorphisms in two autophagy-related genes, ATG16L1 and IRGM, as well as the nucleotide-binding oligomerization domain-containing protein 2 (NOD2) are the key genetic correlations with CD (Hugot *et al*., 2001; Hampe *et al.*, 2007; Parkes *et al.*, 2007; Travassos *et al.*, 2010) [12, 10, 21, 38]. The same is true for UC (ulcerative colitis), where genome-wide association studies (GWAS) have discovered a total of 47 susceptibility loci, including mutations in the extracellular matrix protein 1 (ECM1) and an amino acid variant at position 11 of HLA-DR1 (Achkar *et al.*, 2012; Bamias and Cominelli, 2007) [1, 2]. Th1 cells, which produce more IL2, IL12, and IFN than other types of lymphocytes, predominate in CD (Bamias and Cominelli, 2007) [2] And while UC has historically been seen of primarily a Th2-mediated syndrome, it has recently been realised that IL-13, TNF-like cytokine (TL1A), IL-33, and their receptors play a crucial role in the disease (Cayrol *et al*., 2009; Mannon *et al*., 2011) [5, 18]. Recent data suggests an unique effector route, with the interleukin-23/Th17 axis being its most important component (Sarra *et al*., 2010) [31], may contribute to inflammatory bowel disease-related tissue damage.

2. Dysbiosis and other GI-tract disorders

The intestinal microbiota has been linked to a number of additional (chronic) GI-related illnesses and disorders, including irritable bowel syndrome (IBS), coeliac disease, and colorectal cancer, in addition to IBD, metabolic disorders, obesity, and type 2 diabetes (T2D) (CRC). Different subtypes of IBS have been shown to have altered microbiota compositions when compared to healthy people (Carroll *et al*., 2010; Krogius-Kurikka *et al*., 2009) [4, 16] although the changes are not uniform (Salonen *et al*., 2010) [30]. Additionally, coeliac disease and CRC have been linked to changes in the microbiota's composition, with greater richness and diversity seen when compared to control patients (De Palma *et al*., 2010; Shen *et al*., 2010) [8, 34]. However, no recognisable pattern of microbiota alterations has yet been found in any of these disorders. However, a recent study on the celiac disease has provided new insight into the relationship between host genetics and microbiota makeup in connection to disease development. Coeliac disease is strongly associated with expression of the leukocyte antigen DQ2. Before an illness manifests clinically, children with this haplotype have a different microbiota composition compared to those without HLA DQ2 (Olivares *et al*., 2015) [20]. Some bacterial species have the ability to digest gliadin, which may lessen its immunopathogenicity. Coeliac disease is caused by CD4 T-cell reactivity to dietary gliadin.

Conclusion

In conclusion, it is evident that modifications to the commensal microbiota's structure and composition have an effect on human health. It is unclear if dysbiosis is only a side effect of persistent inflammation or a major cause for pathogenesis. According to the research, the most significant triggering factors for gut dysbiosis are thought to be the modern Western lifestyle and infectious diseases. Changes in the makeup of the gut microbiota may have a significant effect on the development of chronic diseases in genetically vulnerable hosts. According to a recent study, the host's genetic background significantly affects the makeup of the gut microbiota. The scientists demonstrated for the first time that a particular human bacterial association can cause inflammation in

gnotobiotic mice with a particular genetic susceptibility. Therefore, the answer is still not quite obvious as of this writing. We think that whereas gut dysbiosis and genetic vulnerability are closely associated to IBD and other multifactorial illnesses, neither factor alone can cause disease.

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