International Journal of Innovative Studies in Medical Sciences (IJISMS)

ISSN 2457-063X (Online) **www.ijisms.com** *Volume: 3 Issue: 2 | 2019*

Gut Microbiota and the Diseases

Aakriti Tiwari[1#], Priyansha Vashisht[1#], Yogeeta Gupta[1#], Anita Garg Mangla[2*] and Neeru Dhamija[2*]

[1]*Department of Botany, Daulat Ram College, University of Delhi, Delhi, India*

[2]*Assistant Professor, Department of Biochemistry, Daulat Ram College, University of Delhi, Delhi, India*

Email: *neerudhamija83@gmail.com, anitamangla@yahoo.com*

[#]*All three authors have contributed equally to the work and must be regarded as first authors*

[*]*Both authors have contributed equally to the work and must be regarded as corresponding authors*

Abstract: *Human body has lesser human cells and more microbes in their system. Microbes and human cells exist in 10:1 proportions in our bodies. It is 10 trillion human cells versus 100 trillion microbial cells. Thus we are just 10% humans!!!! The entire repertoire of microbes present in an organism is termed as microbiota. Endogenous microbiota is so vast that it's termed as 'microbial organ'. Microbiota exists almost everywhere in our bodies: skin, mouth, vagina, gut. Each point in our body is a microbial community and its dysbiosis (imbalance) leads to diseases. Dysbiosis of microbiota has potential roles in many diseases: Kidney disease in Systemic lupus erythematosus [1], food allergies [2], Ulcerative colitis [3], Crohn's disease [4], cystic fibrosis [5], asthma [6], irritable bowel syndrome [7], obesity [8] and even cancer [9]. The list is large. This review focuses on dysbiosis of the gut microbiota and the associated diseases. A deeper understanding of the gut microbiota will lead us to cures of many incurable diseases which are actually caused due to dysbiosis.*

Keywords: *Microbiota, dysbiosis, IBD, Obesity, Atherosclerosis, colorectal cancer*

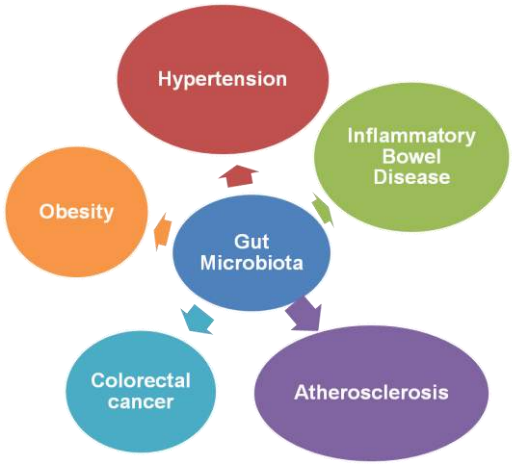

Fig.1. *Gut microbiota is associated with many diseases: Atherosclerosis, Inflammatory Bowel Disease, Obesity, Hypertension and colorectal cancer*

Microbiota develops after birth of the child. Vaginally delivered children versus children born by C-section develop different microbiota. It not only depends on method of delivery but also breast feeding and weaning period. Soon it develops into adult like microbiota which can change with age, environment, body mass index and lifestyle. Gut microbiota can by studied in DNA extracted from poops by 16S rRNA sequencing. 16SrRNA is only present in microbes and not in us. This provides us information about the gut microbiome, which is the collection of genomes from all the microorganisms. The human gut microbiota majorly contains the *Bacteroidetes* and the *Firmicutes*. The homeostasis of gut microbiota is essential for maintaining health of the individual [10]. This review focuses on few diseases when dysbiosis of gut microbiota occurs: Obesity, Inflammatory bowel disease, atherosclerosis and colorectal cancer. We also highlight the plausible importance of fecal microbiota transplant in treatment of these diseases in addition to current therapies being used for additive cure of the disease.

(A) Obesity

A multifactorial disease defined by body mass index greater than 30 kg/m^2. Fat distribution pattern further divides obesity into android and gynoid obesity. Android obesity (apple shaped or central obesity) common in men is more dangerous than gynoid or pear shaped obesity predominant in women. Centrally obese person is more prone to cardiovascular diseases and diabetes type II. Dysbiosis of gut microbiota has been seen in obese person with increased *Firmicutes* and decreased *Bacteriodetes* (Fig. 2). Also, obese people show less alpha diversity of microbes illustrating diverse kinds of microbes is not present in the fecal samples of obese person [11]. Like any multifactorial disorder, dietary changes influence the microbiota to larger extent. For example, change to diet rich in animal fat increases *Bacteriodetes* levels, while switching to diet rich high fat and low fiber decreases plant polysaccharide degrading microbes like *Eubacterium rectale.* Dietary fiber intake improves overall microbiota richness of the gut [11].

Although in its infancy, fecal microbiota transplant (FMT) or bacteriotherapy, a process by which fecal bacteria from a healthy individual is transplanted in intestine of an obese person carry promising therapeutic potential for treating obesity.

(B) Inflammatory Bowel Disease (IBD)

In this disease there is severe inflammation of the gut mucosa. It includes Ulcerative colitis, in which the inflammation is restricted to large intestine (colon) and Crohn's disease in which the inflammation can be in any part of the digestive tract. Dysbiosis plays an important role in the pathogenesis of IBD. Quantitative PCR analysis revealed overall 10-fold reduction in total bacterial load in IBD patients specifically the members of *Lachnospiraceae* and *Bacteroidetes* are significantly reduced [12-17] (Fig. 2).

Antibiotics, prebiotics (dietary supplements supporting protective bacterial growth) and probiotics (live friendly bacteria) are frequently used to gain back our intestinal microflora [16]. FMT is a promising treatment of IBD along with probiotics to regenerate back the gut flora.

(C) Atherosclerosis

Atherosclerosis is one of the cardiovascular diseases which also show signs of dysbiosis apart from genetic and dietary factors. In atherosclerosis, plaques are formed by accumulation of cholesterol and macrophages (foam cells) at the site. Gut barrier protects the gut from the invading pathogens. Gut dysbiosis leads to increase in the intestinal permeability. Lipopolysaccharide (LPS) increases at the site and hence toll like receptor 4. This promotes the development of atherosclerosis. Short chain fatty acids and many other metabolites like trimethylamine N-oxide (TMAO), and secondary bile acids (BAs) by gut microbiota are involved in many diseases including atherosclerosis [18, 19, 20, 21]. Relative abundance of *Roseburia* and *Eubacterium* is decreased while *Collinsella* was increased in atherosclerotic patients compared to aymptomatic healthy controls [21]. Fecal transplantation will help in treatment of atherosclerosis also by introduction of healthy good bacteria.

(D) Hypertension

Hypertension is a term describing the medical condition of 'high blood pressure'. It refers to an increased systolic and diastolic pressure (in resting state). Systolic pressure above 140mm Hg and diastolic pressure above 90mm Hg is a condition of hypertension. Being a complex mechanism, the regulation of blood pressure involves the interaction of multiple physiological systems, such as, the renin–angiotensin–aldosterone system, the sympathetic nervous system (SNS), the nitrate–nitrite–nitric oxide signaling pathway (NO), uric acid, endothelin, the vasopressin system and many more, and is influenced by environment and genes. Many researches on gut microbiota, have demonstrated a significant decrease in microbial richness and diversity in the presence of hypertension.

In a rat model of hypertension, the number of cecal "good bacteria" from the phylum *Bacteroidetes,* is reduced, which is accompanied by a proportional increase in the number of "bad bacteria" from the phylum *Firmicutes*. It has been also observed that there is significant decrease in microbial richness and diversity in hypertension [19, 20, 21, 22].

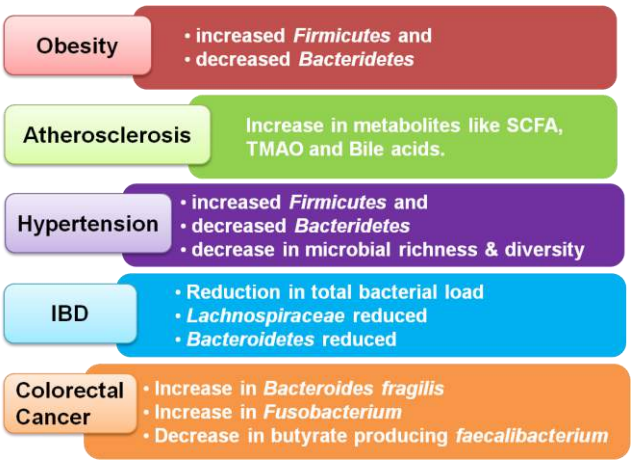

Fig. 2: *Dysbiosis in the gut microbiota and its outcomes are related to diseases.*

(E) Colorectal cancer

Colorectal cancer (CRC) is the gastrointestinal cancer which is multifactorial. Apart from genetic and environmental factors, Sulfidogenic bacteria, such as *Fusobacterium, Desulfovibrio and Bilophila wadsworthia*, have been implicated in CRC development. The production of hydrogen sulphide by these bacteria results in the genotoxicity damaging the DNA and introduction of mutations. *Streptococcus bovis*, a Gram positive organism and *Fusobacterium nucleatum* (*F. nucleatum*) are also linked with CRC. *Bacteroides fragilis* is an anaerobic bacteria commonly found in the human body but its numbers increase in CRC [26, 27, 28] (Fig. 2). These bacteria and their numbers are also influenced by lifestyle and dietary factors such as low fiber foods, consumption of alcohol, smoking and sedentary lifestyle. Other environmental factors that cause dysbiosis are oxidative stress, toxins, virulence factors and inflammation [27]. In normal scenario, commensal bacteria in our gut are detected by host Toll like receptor and NOD like receptors which triggers cytokine release maintaining balance. However, destruction of the tight junction and entry into the inner mucous lining by pathogens are sensed as danger signals. These signals are spread and activate diverse signalling cascades [28].

Conclusion

Microbes play important roles in our body. They provide us with B and K vitamins, help in digestion. They outnumber us in a 10:1 proportion. Thus any changes in their numbers disturb the homeostatis of human body. This omics era-metabolomics, genomics,

proteomics, transcriptomics- is helping us in better understanding of the gut microflora and its association with these diseases. We had an insight into the dysbiosis leading to many diseases. The research on fecal microbiota transplant (FMT) is still in its infancy but shows promising therapeutic potential.

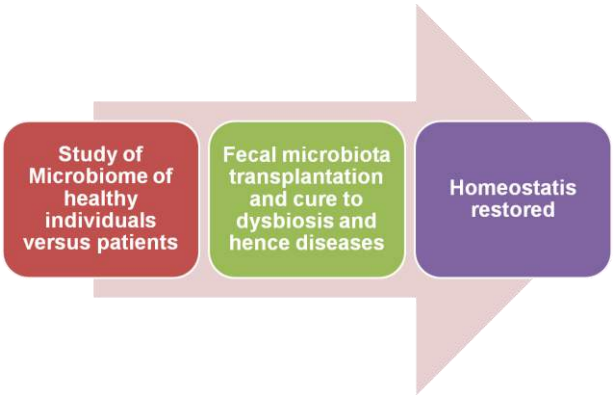

Fig.3. *Gut microbiota: a promising cure to diseases*

Acknowledgements

We would like to express our deep gratitude for our principal, Dr. Savita Roy for her unfaltered support.

References

[1] *Joanna Collison*, Gut microbiota linked to kidney disease in SLE, ***Nature Review Rheumatology***, March 5, 2019

[2] *Supinda Bunyavanich*, Food allergy: could the gut microbiota hold the key? ***Nature Reviews Gastroenterology & Hepatology***, March 1, 2019

[3] *Xiao-Yan Wang etal.*, Relationship between intestinal microbiota and ulcerative colitis: Mechanisms and clinical application of probiotics and fecal microbiota transplantation, ***World J Gastroenterol.***, Jan 7; 24(1): 5–14, 2018

[4] *Ferguson LR etal.*, Role of gut microbiota in Crohn's disease, ***Expert Rev Gastroenterol Hepatol.***, Oct; 3(5): 535-46, 2009

[5] *Putignani L etal.*, Gut microbiota signatures in cystic fibrosis: Loss of host CFTR function drives the microbiota enterophenotype, ***PloS One***, Dec 6; 13(12), 2018

[6] *Kau AL etal.*, The Human Microbiota and Asthma, ***Clin Rev Allergy Immunol.***, Nov; 13, 2018

[7] *Santos J etal.*, A Review of Microbiota and Irritable Bowel Syndrome : *Future in Therapies,* ***Adv Ther.***, Mar; 35(3): 289-310, 2018

[8] *Nie Y etal.*, Insights into the role of gut microbiota in obesity: pathogenesis, mechanisms and therapeutic perspectives, ***Protein Cell,*** May; 9(5): 397-403, 2018

[9] *Arshad M etal.*, Microbiota in cancer development and treatment, ***J Cancer Research Clinical Oncology***, Jan; 145(1): 49-63, 2019

[10] *Lanjuan Li etal.*, The Human Microbiota in Health and Disease, ***Engineering***, Feb; 3 (1), 71-82, 2017

[11] *Dan Waitzberg etal.*, Gut microbiota and obesity, ***Clinical Nutrition Experimental***, Aug., 20, 60-64, 2018

[12] *Pace NR etal.*, Molecular-phylogenetic characterization of microbial community imbalances in human inflammatory bowel diseases, ***Proc Natl Acad Sci U S A.***, Aug 21; 104 (34), 13780-5, 2015

[13] *Lynch SV etal.*, Role of the microbiota in inflammatory bowel diseases, ***Inflamm Bowel Dis.***, May; 18 (5), 968-84, 2012

[14] *Andoh A etal.,* Gut microbiota in the pathogenesis of inflammatory bowel disease*,* ***Clin J Gastroenterol.****, Feb; 11(1), 1-10, 2018*

[15] Tomov VT etal., Gut microbiota and IBD; causation or correlation? ***Nat Rev Gastroenterol Hepatol***, Oct.; 14 (10), 573-584, 2017

[16] *Wirtz S etal.*, The Intestinal Microbiota in Inflammatory Bowel Disease, ***ILAR Journal.***, 56(2), 192-204, 2015

[17] *Guarner F etal.*, The gut microbiota in IBD, ***Nat Rev Gastroenterol Hepatol.***, Oct; 9 (10), 599-608, 2012

[18] *Marostica Junior MR etal.*, Interplay between food and gut microbiota in health and disease, ***Food Res Int.***, Jan; 115, 23-31, 2019

[19] *Lal SK etal.*, The Human Gut Microbiome: A Potential Controller of Wellness and Disease, ***Front Microbiol.***, Aug; 14 (9) 1835, 2018

[20] *Finlay BB etal.*, Gut microbiota in health and disease, ***Physiol Rev.***, Jul; 90 (3), 859-904, 2010

[21] *Houkai Li etal.*, The Role of Gut Microbiota in Atherosclerosis and Hypertension, ***Front Pharmacol***, 9: 1082, 2018

[22] *Cai Y etal.*, Gut microbiota and hypertension: From pathogenesis to new therapeutic strategies, ***Clin Res Hepatol Gastroenterol***, Apr; 42(2): 110-117, 2018

[23] *Shatat IF etal.*, "The Microbiome and Blood Pressure: Can Microbes Regulate Our Blood Pressure? ***Front Pediatr,*** Jun; 19 (5), 2017

[24] *Koichi Node etal.*, Gut microbiota and hypertension, ***Hypertension Research***, Jan; 11, 2019

[25] *Kaye DM etal.* , Beyond gut feelings: how the gut microbiota regulates blood pressure, ***Nat Rev Cardiol.***, Jan; 15 (1), 20-32, 2018

[26] *Kistler CA etal.*, The gut microbiome and colorectal cancer: a review of bacterial pathogenesis, ***J Gastrointest Oncol.***, Aug; 9(4), 769-777, 2018

[27] *Ghasemian-Safaei, H etal.*, Role of gut microbiota in the pathogenesis of colorectal cancer; a review article, ***Gastroenterology and hepatology from bed to bench***, 11 (2), 101-109, 2018

[28] *H. Qin etal.*, Gut microbiota and colorectal cancer, ***Eur J Clin Microbiol Infect Dis.***, 36 (5), 757-769, 2017