

Human Microbiome: Effects on Nutrition and Health

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ABSTRACT

The existence of microorganisms that we share our body has been known for a long time. The human body is a structure that contains both its own genome and the genome of the microorganism community with which it lives. However, changes in our way of life and especially the new molecular compounds we take into our bodies cause various effects on these microorganisms. Recent studies show us that these microorganism communities have more impact than expected on human health. It is clear that illuminating this structure and the interaction between them will make an important contribution to seeing the effect of microbiome on human health and even in determining the treatment of diseases.

INTRODUCTION

All of the beneficial, harmless, and harmful microorganisms that we share our bodies are called the microbiome. Microorganisms make up only 1.2% of the body mass of a healthy person; however, the number of microbial cells in the human body is estimated to be ten times the human cell, and microbial genes are estimated to be 100 times the total human gene. It is known that microorganisms play an important role in the survival of a healthy body, and sometimes they appear as infectious agents. Microorganisms involved in health and disease associated with the human body; eukaryotes, bacteria, and viruses. The research area, which aims to understand the different functions and interactions of microorganisms and how they affect the physiology and health of the host, is called microbiome. Metagenomics' and clinical research work together as a necessity to gather accurate and in-depth information about the correlation between the microbiome, microbiome, and health ^[1].

LITERATURE REVIEW

Microbiome

All of the microorganisms that can be commensal, symbiotic, and pathogenic that we share our bodies are called a microbiome. The microbiome is an active community and plays a complementary role in terms of disease and health. Also, research has been supported by how they play a role in obesity, gastrointestinal system, the immune and mental system for the pediatric population. The Human Microbiome Project (HMP) reflects the fact that we are

a superorganism formed by the combination of human and microbial components. The Human Microbiome Project is a global project designed to understand microbial components genetically and metabolically, to understand the impact of the microbiome on human physiology and human affinity to diseases, and aims to break down artificial barriers between medical and environmental microbiology. The objectives of the project are; to identify variations in human microbiome-based on genotype, age, nutrition, disease, drug use, and environmental factors while creating standard data sources using high-capacity new technologies such as metagenomics sequencing. The main purpose of the project can be summarized as creating wide possibilities to improve human health by closely monitoring and interfering with the human microbiome. Obesity, metabolic syndrome, and diabetes are important public health problems affecting approximately 26 million children and adults in the USA. More than 8% of the U.S. population has diabetes, and 17.9 million people have metabolic syndrome. Therefore, interest in the possible role of the intestinal microbiome in obesity prevalence is rapidly increasing.

Microbial Flora (Microbiome-Microbiota) Residential Areas

The mucosa of the surface, cavity, and organs associated with various connections with the skin, mouth, throat, intestine, nose, urogenital regions, external environment, in general, of the settlement areas of the microorganisms in the human body it is known to have membranes. Normal flora members, in various parts of our body, varies depending on age, gender, hormonal changes, nutritional characteristics, and personal habits.

The flora carried in the body throughout human life continues to change depending on the situation. These organisms can be colonized temporarily or permanently colonized in the person; it may also cause disease. Normal microbial flora; It can be examined in two groups as permanent flora and temporary flora. Permanent flora; It is a community of microorganisms that do not change in certain regions, can be reconstructed even if it is eliminated for a short time and shows continuity. Temporary flora is a collection of microorganisms, which are not permanent, but can be pathogenic, and may vary from a few hours to several weeks. When permanent flora members disappear, the temporary flora will colonize, multiply, and become disease-causing [2].

DISCUSSION

Antibiotics are the cornerstone of the treatment of infectious diseases. However, bacterial resistance to antibiotics has increased over time and continues to increase. It is understood that antibiotics exert two different effects on intestinal microbiomes with increasing knowledge about the intestinal microbiome. Antibiotics can destroy useful bacteria while destroying pathogenic bacteria. Also, even if absorbable antibiotics are applied for diseases that do not concern the intestine due to their distribution in our body, it affects microbial flora. This phenomenon disrupts the intestinal microbiome and increase of related diseases. Besides, the disruption of the microbiome due to antibiotic therapy may lead to increased antibiotic resistance.

Researchers have observed taxonomic changes within the microbiome, changes in the growth of important key genes involved in carbohydrate metabolism, increases in short-chain fatty acid levels, changes in the regulation of liver metabolism of lipids, and cholesterol. In this study, they treated young mice with antibiotics. As a result, the evaluation of the changes in the composition and capacity of the intestinal microbiome and the intestinal flora of the mouse were damaged in antibiotic treatment method, the young mouse's adipose tissue and hormone level increased with this metabolism.

In another study, microbial flora resistances of healthy individuals were examined to investigate the effect of antibiotic-resistant genes on human pathogens. Many of the resistance genes are different from the previously known resistance genes determined by independent sampling. However, approximately half of the resistance genes detected in culture aerobic digestive isolates (a small subset of the digestive system microbiome) are identical to the resistance genes that are bound by important pathogens. This large diversity in human microbiome resistance genes can contribute to antibiotic resistance to human pathogens [3].

As a result of antibiotic treatment, undesirable effects detected in bacterial ecology occur. That is defined as "collateral damage." Examples of collateral damage, which are closely related to inappropriate antibiotic use, are indicators that should be taken into consideration while determining antibiotic use policies in the hospital and community. With better antibiotic management, it will be possible to reduce collateral damage and increase the benefits of antibiotics.

It is vital importance to maintain a bi-directional signal balance between the gastrointestinal tract and the brain, and this balance is regulated by the neural (together with the central and enteric nervous system), hormonal and immunological levels. Stress response and general behavior changes cause anxiety as a result of these systems. It

is evidence of the importance of this axis that there is a relationship between stress-related psychiatric symptoms, such as high comorbidity (simultaneous occurrence of many additional diseases along with the basic disease) and sensitive bowel disorder (spastic colon) and inflammatory bowel disorder. It shows that the stages of enteric microbiomes on intestinal brain communication affect the enteric microbiota greatly. Mechanisms governing this type of communication are studies that focus more on the effect of uncertainty and the effect of the signal change from the brain to the gut. New studies have investigated the effects of intestinal microbiomes on the brain and microbiome. Because it reveals the role of intestinal microbiota on brain function, cases such as prebiotic agents, antibiotic-impaired body's impaired microbial balance, and the effect of pathogenic infections are evaluated. Since the intestinal microbiome can communicate with the brain, it is an important concept for the health and disease of our body, which can be effective in individuals' behavior.

Despite the negative effects of the absence of intestinal flora, the intake of beneficial bacteria through food can play role in improving the normal balance in the gut and improving health. It is known that food components called prebiotics, which do not contain bacteria, but help reproduce beneficial bacteria, have important effects on the formation of intestinal flora. Nutrition with a herbal-weighted diet promotes the formation of a more favorable intestinal microbial profile. Dietary fiber and fermented substrate, which are generally abundant in such diets, namely undigested or undigested carbohydrates, are used as nutrients for microbial development in the gut. Modification of the intestinal microbial content remains an option in the treatment and management of chronic diseases in recent years.

Probiotic bacteria play a role in balancing the immune system. They also compete with microorganisms that are harmful to the body and help prevent them from entering the circulatory system from the intestinal epithelium. In immune system diseases, the gastrointestinal tract needs to be supplemented with probiotics.

The effects of probiotics on the immune system can be listed as follows: direct regulation of the immune response, strengthening the barrier function on the intestinal surface and suppressing the growth of disease-causing microbial agents, thereby maintaining the immune balance. Also, these microorganisms have both protective and therapeutic properties against allergic diseases. For example, it has been shown in many studies called "atopic dermatitis," where contact-related allergies have been successfully treated with the use of probiotics. Probiotics are successful in the treatment of upper respiratory tract infections such as influenza, colds, sinusitis, otitis media, and have a protective effect against these diseases. Besides, probiotics have been used in the treatment of lower respiratory tract infections such as pneumonia and bronchitis, and very successful results have been obtained. It has also been proven that probiotics reduce the chance of contracting these diseases and show protective effects. In the studies, it has been observed that the probiotic structure in the intestines of autistic children is impaired, and it is determined that probiotic supplementation is important in treatment. It has been observed that the structure of probiotics is disturbed in high blood pressure and diabetes. It is stated that these patients have an important benefit in supplementing probiotics [4]. Probiotics help digest food by breaking down cellulose and other no digestible food components in the intestines and assist nutrition and growth by ensuring a healthy metabolic activity. Probiotics help the formation of intestinal microflora, which is impaired in newborns, using antibiotics or depending on the conditions of daily life. Probiotics also prevent the breakdown of intestinal microflora by controlling the growth of unwanted bacteria, yeasts, and molds. It has been stated that the consumption of specific lactic acid bacteria strains increases the production of peptides that increase immunity, and some of them have an inhibitory effect on tumor formation. When probiotic bacteria are found insufficient numbers in the intestinal flora, it is stated that they synthesize vitamins and amino acids. The most important of the vitamins produced by these bacteria are thiamine (B1), riboflavin (B2), pyridoxine (B6), and naphthoquinone (K).

The effects of microbiome on human health

In recent studies, it has been suggested that the intestinal microbiome performs very important biochemical events for the host and is associated with various human diseases. With the new generation of "OMICS" technologies, the importance of the intestinal microbiome in human health, its genetic and functional levels can be defined in detail, and the variability of the microbiome between individuals can be examined. Thus, understanding the activity of the microbiome is very important for both future health development and can open new horizons for drug development methods. Studies are underway to understand human health-related gut microbiome activity for the treatment of human disease. Research has proven that food components are associated with diseases such as intestinal diseases and diabetes. Phosphatidylcholine, fat-enriched L-carnitine, some fatty acids, and their products found in western diets support the formation of diseases affecting chronic intestinal disease and arteries. In contrast, carbazoles or proteins enriched in tryptophan reduce the occurrence of disease. If the "microbiome-immune-diet" interaction can be fully understood, many diseases can be treated by developing food-based approaches.

Bacteria can have complex relationships with other organisms. These relationships are known as symbiotic. These symbiotic societies can be divided into intrusion, exchange, and commitment. Thanks to these communities, these bacteria can grow almost anywhere. For example, it may develop on the skin, increase the body temperature in humans and cause sweating and, ultimately, body odor. Some bacterial species kill other microorganisms. Another group of harmful bacteria is species that inhibit the absorption of food or digestion. Mutualism is a common way of life, based on mutual assistance of two living creatures of different species. Some bacteria form communities of mutualism that are necessary for their own life. For example; Other Archaea-related bacteria that only consume hydrogen keep the ambient hydrogen level at a level that only Archea can survive. The presence of almost a thousand species of bacteria that can be found in the normal human intestinal flora can contribute to the immune system by providing the synthesis of some vitamins.

On the other hand, lactic acid synthesis increases the acidity of the medium. This prevents the development of potentially pathogenic bacteria in the intestinal flora, often through competitive exclusion. These beneficial bacteria are sold as probiotics supplements.

It has been proven that the fact that some antidepressants cause more depression instead of benefit has been related to the variety of gut bacteria. Thereupon, the results were very successful when the antidepressant was cut, and the patients were given yogurt containing *Bifidobacterium long* NCC3001.

Disorders in the variety and rate of bacteria in the gut can cause other disease-causing bacteria to dominate the body. Also, a bacterium (*Bacteroides fragilis*) seen in 15-20% of people is effective in the treatment of many diseases ranging from Alzheimer's to Multiple Sclerosis (MS).

Genetic Disorders

Some genetic disorders and learning difficulties have been observed in young children with intestinal flora disorders. It has been shown that some of these problems can be corrected by living bacteria taken as tablets.

Diabetes

It is known that the intestinal flora of diabetics is different from healthy individuals. Research continues on the effect of regulation of diabetic gut bacteria on health. The most used bacteria for this are; *Bacteroides* are Proteobacteria and Firmicutes.

In studies conducted for obesity disease, it has been observed that traditionally grown mice have 40% higher body fat content, although their food consumption is less than gnotobiotic mice. The intestinal microbiome of traditionally grown young and mice were transferred to gnotobiotic mice, and a 60% increase in body fat was observed within two weeks. However, there was no change in food consumption and energy expenditure. The increase in body fat caused an increase in insulin resistance and increased blood glucose concentration. These studies show that the microbiome supports the absorption of monosaccharides from intestinal and liver-derived lipogenesis. In one study, a 32-year-old woman fell ill due to *Clostridium difficile*. In this person, the treatment of stool transplantation, which has become increasingly widespread in recent years, has been tried, and fecal transplantation has been performed from his daughter. It has been observed that the woman has recovered as a result of the transplant. It was also determined that the 32-year-old woman was at a normal weight before transplantation, and her body mass index was at the level of 26 (healthy value range). However, it is known that the girl who took feces had a weight problem. It was observed that the 32-year-old woman started to gain weight rapidly and progressed to obesity after the transplant. Doctors who see this result think that the natural flora from their daughter during stool transplantation causes obesity. In studies on artificial sweeteners (for example, saccharin), it was concluded that these sweeteners worsen metabolic disorders. The mouse fed saccharin was unable to tolerate glucose compared to that fed only glucose. The researchers took the gut content of the mouse that could not tolerate glucose and transported it to the other mouse, and the transplanted mouse was unable to digest the glucose. These results show that artificial sweeteners cause the microbiome to become unhealthy and eliminate its digestive aid effect, leading to metabolic disorders, causing obesity.

Although thousands of researches on autism offer different suggestions, some researchers show that the intestinal bacterial flora is impaired during the development of the baby; the immune system is disrupted. The brain is affected afterward. Researchers focused specifically on the potential role of intestinal microbiota in the autism mechanism. It is being investigated that *Clostridium boltonii* is significantly more common in the intestine of autistic children and whether the intestinal flora is effective on the onset of autism.

The dominant bacteria found in recent research in patients with colorectal cancer have been identified using the 16S rDNA DGGE analysis. *Clostridium leptum* diversity and *Clostridium coccooides* subgroups were also found in patients. *Desulfovibrio* spp. were found to be less than other microorganisms but significantly higher than healthy individuals. These bacteria are thought to increase colorectal cancer.

Studies have suggested the contribution of environmental factors in the development of allergies and asthma during infancy. Environmental factors shape the intestinal microbiota. Intestinal microbiota also shapes the development of intestinal functions. Differences in these gut functions also affect the intensity and content of the response to viruses and allergens encountered. A different view is that the respiratory system is somewhat more suitable for microbial colonization. Another view is that microorganisms may have inhibited allergic sensitivity. In studies in newborn babies, findings indicating that this situation increases in regions with high rates of poverty have been reached. There is still an ongoing study on whether the hygiene hypothesis is valid. The children who spent more than three years of their lives collecting garbage were analyzed from a bacterial point of view, and high sensitivity and virus-triggered wheezing were observed in these children. Even though cockroaches, cats, allergens and bacterial diversity are very low, high rates of allergic sensitivity and repetition of these children were observed in the first years of their lives. In contrast, wheezing has been observed in those more exposed to these allergens and high bacterial diversity. Recent studies have emphasized that commensal bacteria may protect against allergens in foods [5].

In recent years, fecal microbial transplantation has been investigated in the treatment of recurrent *C. difficile* enteritis. In a study conducted in a center where this treatment was applied, 79% of the total of 75 fecal microbial transplantation treatments in 9 years have been successful. Nine of the 16 cases whose diarrhea continued were healed with single-dose antibiotic (vancomycin) treatment. As a result, the decrease in the number of *Clostridium difficile* has been effective in healing patients with diarrhea.

CONCLUSION

There are many more microorganisms in the human body than the number of cells. It is known that its number can be up to 100 trillion, its weight is about 2 kg and belongs to at least 300-1000 species. Especially in recent years, it has been revealed that imbalances in the structure of the microbiome (dysbiosis) may be related to some diseases. It is also seriously emphasized that the postpartum microbiome of newborn babies may be associated with future diseases. Even though it is not directly related to our subject, it is also emphasized that there may be an important connection between the microbial structure of the soil in which the plant roots are located and the plant productivity. It was proved by Barry J. Marshall and J. Robin Warren that his ulcer disease was caused by a bacteria living in the stomach (*Helicobacter pylori*), and their Nobel prize in 2005 opened up new horizons in the scientific world and studies on the relationship between the causes of many diseases and microorganisms in the body accelerated. For example, in the new studies, the treatment rate of the disease was found to be much higher in the use of probiotics containing *Lactobacillus* and *Bifidobacterium* in the treatment of ulcers with antibiotics compared to the control group. It has been demonstrated that the reason for this is that bacteria producing lactic acid decrease the urease activity of *H. pylori*, which causes the disease, and probiotics have been added to the treatment protocols. The metabolites created by human enzymes are different from the anaerobic microorganism metabolites, and therefore studies have always carefully examined how diet affects microbiome. Perhaps the methods used to treat some diseases today will be replaced by a controllable microbiome in the future. Based on all these data, doctors express this situation as well as our microbes. As a result, it would not be wrong to say that we are at the very beginning of host microorganism relationships.

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