INTERNATIONAL MULTI DISCIPLINARY JOURNAL FOR RESEARCH & DEVELOPMENT
eISSN 2394-6334 Impact factor: 8.854 Volume 13, issue 06 (2026)

BRIEF ANALYSIS OF THE IMPORTANCE OF MICROBIOTA IN ENSURING HUMAN HEALTH AND THE OCCURRENCE OF DISEASES

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Abstract. The term "microbiome" typically refers to the population of different microorganisms that reside on the skin or inside the bodies of humans and animals. Trillions of commensals, symbiotics, and even harmful microbes make up this intricate ecology. The main factors affecting the composition and vitality of the microbiome include diet, lifestyle, and the external environment. The microbiome has a huge impact on both health and illness, according to recent research. They are dynamic in terms of quantity, composition, diversity, and viability. Since its discovery, several studies have emphasized the importance of microbiota in health and disorders. Microbiota can be categorized as gut, oral, respiratory, and skin microbiota based on the localized areas. In symbiosis with the host, the microbial populations provide immunological regulation and homeostasis. However, dysbiosis of the microbiota can result in dysregulation of physiological processes and illnesses such as cancer, respiratory disorders, cardiovascular diseases (CVDs), etc. Numerous health issues are caused, developed, and treated by all of these factors. Microbiota can have a direct or indirect impact on serious conditions like cancer, metabolic disorders, cardiovascular diseases, and even psychological disorders like schizophrenia. The present understanding of the relationship between microbiota and host health or disease is covered in this review. First, we provide an overview of the research on the gut-brain axis, colonization resistance, and immunological regulation of microbiota under healthy conditions. Next, we discuss the pathophysiology of microbiota dysbiosis in the onset and course of disease, which is mainly linked to dysregulation of community composition, host immune response modulation, and chronic inflammation induction. Lastly, we present therapeutic methods including fecal microbial transplantation and microbiota manipulation that use microbiota to treat diseases.

Keywords. Microbiota, Virome, Virobiota, Bacteriophages, Health, microbial communities, skin microbiota.

Introduction. The term "microbiota" first appeared in the early 1900s. Numerous microorganisms, such as bacteria, yeasts, and viruses, have been discovered to dwell in different parts of the human body, such as the mouth cavity, lung, skin, and stomach. Furthermore, the human microbiota—also referred to as "the hidden organ"—contributes more than 150 times as much genetic information as the entire human genome. Despite their frequent interchangeability, the terms "microbiota" and "microbiome" differ in a few ways. The live microorganisms present in a specific environment, such as the oral and intestinal microbiota, are referred to as microbiota. The term "microbiome" refers to the collection of genomes from every microbe found in the environment, which encompasses not only the microbial population but also the microbial structural components, metabolites, and environmental factors. In this sense, the scope of the microbiome is wider than that of the microbiota. The role of microbiota in human health and illness is the primary topic of this review. Every site has a different microbial composition. The gut microbiota is thought to be the most important for preserving human health. The gut bacteria perform a number of tasks, including food fermentation, pathogen defense, immune response stimulation, and vitamin synthesis [1-5]. *Firmicutes, Bacteroidetes, Actinobacteria, Proteobacteria, Fusobacteria, and Verrucomicrobia* are the two main phyla that make up the gut microbiota. *Candida, Saccharomyces, Malassezia, and Cladosporium* are the most researched

fungus (gut mycobiota). The human gut microbiota includes phages, viruses, and archaea, primarily M. *smithii*, in addition to bacteria and fungi. Microbiota is also found in other areas, such as the skin, oral cavity, lung, and vagina, albeit it is less well-established than in the stomach. The second-largest microbial population in humans is thought to be the oral microbiota. Saliva, tongue, tooth surfaces, gums, buccal mucosa, palate, and subgingival/supragingival plaque are just a few of the oral cavity's many microbiota habitats. These habitats can undergo significant and quick changes in composition and activity due to things like pH shifts, gene mutations, and bacterial interactions. Although there are some variations, the microbiota makeup in each of the seven locations is generally comparable. *Firmicutes, Proteobacteria, Bacteroidetes, Actinobacteria* and *Fusobacteria* are often the main bacteria found in oral microbiota. Numerous investigations have shown that microbiota is also present in lung tissues, despite the long-held belief that healthy human lungs are sterile [6-11]. *Actinobacteria, Bacteroidetes, Firmicutes, and Proteobacteria* comprised the core lung microbiota. Three main factors influence the composition of lung microbiota: 1) microbial immigration; 2) microorganism elimination; and 3) microorganism reproduction rates. Each geographical area has a different distribution and variety of glands and hair follicles in human skin. Different skin regions have different microbiota compositions due to their physical and chemical variations. *Actinobacteria, Bacteroidetes, Cyanobacteria, Firmicutes* and *Proteobacteria* typically make up the skin microbiome. Researchers have spent a lot of money studying the human body's microbiome. These microbes are essential to both immunity and illness. Of which, probiotics are live beneficial microorganisms that keep your intestinal or lung microbiota healthy, and occupy a special role in combating the infections. Understanding their contributions to these processes is so crucial. Advanced research on the microbiota, including its development and both beneficial and detrimental impacts on the immune system, can be made easier by technology. This study examines the effects of several factors on the microbiota, especially in the early stages of life, including the manner of administration, metabolic processes, microbe species, and immune system interactions. Additionally, the research explores the potential link between gut microorganisms and certain disease processes, including those associated with diabetes, autism, and schizophrenia [12-19]. Clinical studies show that certain probiotic strains, like *Lactobacillus rhamnosus* GG and *Bifidobacterium animalis ssp*. lactis help to prevent infection of pathogenic organisms (both bacterial and viral). Important advances in public health and disease prevention could result from this research. Later on, the acquired immunity may vary due to the dysbiosis. By lowering proinflammatory cytokines, the probiotic strains can stop viral replication during COVID-19 or SARS-CoV-2 infection. The diversity, volume, and potential function of gut flora in illness have sparked a lot of curiosity. Future studies in the field of microbiome should be conducted to determine their relationship to gut virome by observing their mutual influence as well as pertinent health and illness. The connection between microbiota and illnesses like cancer, diabetes, and neurological conditions has been extensively studied in the past few decades. Furthermore, modifying the human body's microbiota may be essential for treating illness. Here, we provide an overview and discussion of our current understanding of human microbiota's role in disease formation, health condition mediation, and prospective therapeutic applications [20-25].

The main purpose of the submitted manuscript is to provide a brief analysis of the importance of microbiota in ensuring human health and the occurrence of diseases, based on the results of authoritative scientific works.

The intestinal microbiota that is "healthy." Intestinal microbial balance is closely relevant to human diseases and health. The human gastrointestinal (GI) tract is home to over 100 trillion bacteria, making it a more abundant microbial ecosystem than other parts of the body.

Numerous investigations have demonstrated the crucial connection between gut bacteria and fundamental human biological functions. For instance, recent research has demonstrated the strong relationship between human microbiota and immunity, metabolism, and nutrient extraction. Microbiota can influence biological processes in a number of ways. The microbiota is essential for the extraction of nutrients and energy from food because of its diverse metabolic genes that produce distinct, independent enzymes and biochemical pathways. Furthermore, the gut microbiota plays a major role in the creation of bioactive compounds like vitamins, lipids, and amino acids. In terms of the immune system, the human microbiota plays an important role in the development of the intestinal mucosa and immune system in addition to protecting the host from foreign pathogens by generating antimicrobial compounds [6-12]. The gut microbiota shows resilience, stability, and symbiotic relationship with the host under normal circumstances. The notion of a "healthy" gut microbiota and its connection to host physiological processes have been extensively studied. Bacteria, yeasts, and viruses make up the gut microbiome. High taxonomic diversity, high microbial gene richness, and a stable core microbiota are frequently seen in a healthy microbiome community. It should be highlighted, nonetheless, that the relative distribution of microbes varies from person to person and even within the same person. Age and environmental factors (such as medication use) can affect a person's gut flora. Additionally, distinct GI tract anatomical regions have varied gut flora. For instance, the colon does not include *Proteobacteria* like *Enterobacteriaceae*, which are prevalent in the small intestine. Instead, *Bacteriodetes such as Bacteroidaceae, Prevotellaceae* and *Rikenellaceae* are often found in the colon. Research on the human microbiota is expanding beyond compositional studies and member relationships because the microbiota is crucial to human health and actively participates in a number of biological processes and disease development. In particular, the explanation of the causality of microbiota functions has received greater attention, particularly with the emergence of novel methods like as high-throughput sequencing and interactive modeling and simulation of microbiota. All things considered, more research is still required to fully understand the functions of human microbiota in order to facilitate the advancement of microbiome-based diagnosis and tailored therapy [14-21].

Eubiosis of the human gut microbiota is important. Extensive clinical research on microbiota and their role in eubiosis and associated pathophysiological features is available. Both healthy and ill conditions have been found to have different gut microbiota compositions. Eubiosis conditions are effective in controlling various diseases caused by microbes. The development of eubiosis and the proper consumption of a nutritious food are beneficial to human health. An imbalance in the gut flora brought on by excessive antibiotic consumption promotes systemic illnesses. Numerous population-based studies have demonstrated the extremely advantageous role of the human gut microbiota in healthy individuals, as well as the significance of comprehending its structure and the variables that affect its composition, including food, age, location, systemic illnesses, and medications. The substantial resident bacterial populations in the gut microbiome are attributed to the phyla *Firmicutes, Bacteroides, Actinobacteria, Proteobacteria* and *Verrucomicrobia*. Describing the balanced composition of gut microbiota and disease-related changes is the first step in determining the symbiotic relationships between intestinal microorganisms and their hosts [3-11]. In a healthy state, the microorganisms live in mutual association with the host, influencing the host's health through regulating nutrition metabolism, protecting against infections, and sending signals to immune cells to support host physiology and immunity. Due to difficulties in cultivating some microorganisms, a number of vivo and ex vivo investigations have reported an initial underestimation of the overall number of microbial species in the intestine. Digestion of carbohydrates, gut microbiota, immune system control, and protection against pathogen colonization are all aided by bacteria and proteobacteria.

Microbes in the intestinal system mostly rely on food substrates that are not digested in the upper digestive tract for survival. Human health depends on a healthy balance between the host and gut flora; disruption of this balance is associated with a number of diseases, including diabetes, IBD, obesity, hypertension, and cardiovascular disorders. In order to close the knowledge gap regarding the microbiome-host interaction, its involvement in disease pathogenesis, and its therapeutic significance, human microbiome study is still in its early stages. Therefore, more thorough investigation is required to fully understand this intriguing but mysterious field of study [14-22].

The gut microbiota's composition. Ten years ago, culture-based methods accounted for the majority of our understanding of gut microbiota. The composition of the gut microbiota has been isolated, identified, and counted using traditional culture-based methods. However, because most gut microbes are anaerobic, these methods can only isolate 10–25% of the microbiota.Thus, gut microbiota analysis is done using anaerobic culturing methods, however these methods take a lot of time. Our knowledge of the gut microbiota has greatly increased in recent years thanks to the application of culture-independent techniques, such as high-throughput, inexpensive sequencing techniques. Bioinformatics analysis and 16S ribosomal RNA (rRNA)-based bacterial gene sequencing are used in the research of gut microbiota. All bacteria include the bacterial 16S rRNA gene, which is used to differentiate between species. Another quickly expanding field of study in gut microbiota is metabolomics, which examines tiny chemicals associated with the interplay between bacterial and human metabolism that may have consequences for both health and disease states. It has been found that the GI tract contains more than 1014 bacteria [6-13]. However, according to a recent estimate, the ratio of human to bacterial cells is approximately 1:1. Bacteroidetes, Actinobacteria, Firmicutes, and Proteobacteria are the most common phyla among the ≥1000 bacterial species that make up the gut microbiota. Ninety percent of the gut microbiota, which is most prevalent in a healthy gut, is composed of Firmicutes and Bacteroidetes. Prevotella and Bacteroides are two of the Bacteroidetes genera. Bacillus, Lactobacillus, Ruminicoccus, Enterococcus, and Clostridium are among the more than 200 genera that make up the phylum Firmicutes. Escherichia, Akkermansia, and Bifidobacterium are among the less common taxa. Nonetheless, the makeup of the gut microbiota varies significantly between individuals. Furthermore, because differences in taxa are linked to host function and health, the quantity of both common and rare taxa does not reflect their functional significance. It should be noted that it is difficult to precisely identify and explain the makeup of the gut microbiota in healthy persons due to substantial inter-individual variance, study methodology, and participant recruitment. Additionally, the estimated gut microbiota composition is derived from fecal samples, which do not accurately represent the GI tract's overall gut microbiota diversity [15-25].

Dietary Effects on Gut Microbiota. One of the most researched elements is food, which is believed to be responsible for at least 20% of microbial structural differences. This suggests that dietary treatments may be used to treat diseases by altering gut microbiota. Furthermore, it has been found that the microbial composition is correlated with food habits. The composition of the gut microbiota is believed to alter quickly at the species and family level within 24 to 48 hours after the introduction of dietary interventions because gut bacteria are purged in large quantities and can double in number in an hour. Studies employing mouse models that showed changes in gut microbiota within a day of adjusting macronutrient diet have revealed similar findings. The diversity of gut microbiota has been shown to be quickly altered by short-term, dramatic dietary treatments, although these changes were transient and only lasted a short time [3-8]. Thus, food habits over an extended period of time may have a significant impact on gut flora. Reduced activation of pathways involved in endotoxin generation and stool inflammatory indicators, as

well as a lower prevalence of opportunistic bacterial clusters, are linked to habitual dietary patterns high in legumes, bread, fish, and nuts. Across all cohorts, consumption of essential elements of the Mediterranean diet, such as nuts, fatty fish, fruits, vegetables, cereals, and red wine, is linked to higher abundances of beneficial commensals such *Roseburia, Faecalibacterium* and *Eubacterium spp*. The makeup of breast milk and how it affects the composition of the gut microbiota are topics of growing interest. The billion-dollar infant formula market is one of the key causes of this. When compared to infant formula-fed children, the intestinal microbiota of breastfed children has less microbial diversity and is dominated by *Bacteroide, Lactobacilli* and *Bifidobacteria*. HMOs are the third most prevalent dietary component of breast milk and are prebiotics that are not broken down by pancreatic enzymes. In the large intestine, HMOs encourage the growth of Lactobacillus, Bacteroides, and Bifidobacteria. Furthermore, SCFA generated from the breakdown of HMOs is utilized as a source of energy and lowers luminal pH, preventing pathogen colonization [20-26].

Discussion. Since its discovery, several studies have emphasized the importance of microbiota in health and disorders. Microbiota can be categorized as gut, oral, respiratory, and skin microbiota based on the localized areas. In symbiosis with the host, the microbial populations provide immunological regulation and homeostasis. However, dysbiosis of the microbiota can result in dysregulation of physiological processes and illnesses such as cancer, respiratory disorders, cardiovascular diseases (CVDs), etc. Although all clinical elements of current microbiome research cannot be covered in this review paper, it is highly likely that focused therapies will become clinically significant in the future, particularly in the treatment of chronic diseases across a variety of disciplines. Therefore, as demonstrated for the ICI, microbiome therapies can either be used as a stand-alone treatment for disorders or as an adjuvant that increases the effectiveness of a recommended pharmaceutical agent. In the future, clinicians will be able to use both the bacteria themselves (for example, as advanced pre- or probiotics) and purified or industrially produced molecules as therapeutics (also known as post-biotics) thanks to the identification of functional active bacterial metabolites (such as SCFA or agmatine) by contemporary metabolomics technologies [3-14]. Additionally, doctors will be able to modify the microbiome where it is localized, preventing degradation or alteration in the upper intestinal tract, thanks to the development of GMP delivery systems (such as CIR-NA) that transport bacteria and/or metabolites into the terminal ileum or the colon. But during the past ten years, it has also been evident that since the microbiome is altered differently in various disease situations, such as CD and type 2 diabetes, tailored therapies will need to be developed for specific diseases. Even while the data thus far is highly encouraging, more research, particularly in people, will be crucial to eventually implementing targeted microbiome medicines into clinical practice. In conclusion, a great deal of study has demonstrated how certain microbes cause illnesses while others improve immunity, metabolism, and digestion. The human microbiome's bacteria are essential to immunological processes and illnesses. The microbiota develops throughout life, starting in gestation. Numerous factors, such as food, ambient conditions, and mode of distribution, affect its composition and immunological efficacy [17-22]. Food items and direct microbe intake are two examples of the origins of microbiota. It is conceivable that the gut virome plays an unidentified role in disease pathways. Furthermore, the diversity of gut bacteria and fungi must be investigated concurrently with the human gut virome. In order to better understand bacteria-virus interactions, cell-to-cell connections, virus attachment sites, replication, and the function probiotics play in our gut's defense against viral infections, further research is required. Knowing how these bacteria interact with disease processes may help develop preventative and therapeutic approaches for a variety of conditions, including diabetes, autism, and schizophrenia. The present understanding of the relationship

between microbiota and host health or disease is covered in this review. First, we provide an overview of the research on the gut-brain axis, colonization resistance, and immunological regulation of microbiota under healthy conditions. Next, we discuss the pathophysiology of microbiota dysbiosis in the onset and course of disease, which is mainly linked to dysregulation of community composition, host immune response modulation, and chronic inflammation induction. Lastly, we present therapeutic methods including fecal microbial transplantation and microbiota manipulation that use microbiota to treat diseases [23-26].

Conclusions. We have gradually discovered a new role for bacteria in health and illness after decades of investigation. It is now established that nearly every element of the host can be impacted by microbiota, and that a wide range of illnesses are linked to its dysbiosis. We can now closely examine how bacteria contribute to pathogenesis and preserve human health thanks to cutting-edge research methods. However, the bacterial component of microbiota is the primary focus of research; the significance of viruses, fungi, and other microorganisms in health and illness is still mostly unclear. Furthermore, whereas microbial dysbiosis is frequently seen in illness conditions, the microbiota's causal involvement is yet unknown. As a result, there are still many unanswered questions in this area. The development of microbiota-based treatments like FMT and bacterial modulation has been made possible by a better knowledge of the host-microbiota interaction.

When it comes to treating conditions like diabetes, inflammatory bowel disease, C. difficile infection, etc., these approaches are well on their way to attaining the best possible therapeutic outcome. In conclusion, by manipulating the microbial symbionts, we are now better equipped to cure illnesses and promote health. It is quite likely that tailored therapies will become clinically significant in the future, particularly in the treatment of chronic diseases across multiple disciplines, even if this review paper cannot cover every therapeutic aspect of current microbiome research.

Therefore, as demonstrated for the ICI, microbiome treatments can either be used as a stand-alone treatment for diseases or as an adjuvant to increase the effectiveness of a recommended pharmacological drug. In the future, clinicians will be able to use purified or industrially produced molecules as therapeutics (also known as post-biotics) in addition to the bacteria itself (such as as advanced pre- or probiotics) thanks to the identification of functional active bacterial metabolites (such as SCFA or agmatine) by contemporary metabolomics technologies.

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