ORIGINAL RESEARCH PAPER

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UNRAVELING THE MICROBIAL SYMPHONY: A COMPREHENSIVE REVIEW ON THE HUMAN MICROBIOME AND ITS IMPACT ON HEALTH AND DISEASE

KEY WORDS: Microbiome, Maternal-neonatal microbial bond, Emerging trends

Dr. Niya Roy MBBS, Junior Resident in Microbiology

Dr. Vandana Verma MD, DHA, HOD & Professor, Department of Microbiology, CMC Ludhiana

ABSTRACT

This extensive review provides an in-depth exploration of the human microbiome's dynamic ecosystem, highlighting the diverse microorganisms that contribute significantly to overall health. Factors such as diet, genetics, and medical interventions shape the microbiome, fostering continuous evolution throughout an individual's lifespan. The review elucidates the intricate connections between microbiota and immune responses, emphasizing the crucial maternal-neonatal microbial bond and the impact of lifestyle on microbiota composition. Moreover, disruptions in the microbiome are associated with various diseases, including cardiovascular diseases and cancer. The article underscores emerging trends, calling for intensified research to unveil the microbiome's vast potential, particularly its systemic influence and therapeutic implications. Emphasizing the microbiome's relevance beyond the gastrointestinal tract, the review advocates for the integration of microbiome assessments into clinical practice, paving the way for personalized medicine and transformative healthcare strategies.

INTRODUCTION

The human microbiome, a critical concept in biological research, encompasses a myriad of microorganisms, comprising bacteria, viruses, fungi, and other microbial entities that inhabit diverse regions of the human body. These microorganisms colonize surfaces such as the skin, oral cavity, respiratory and gastrointestinal tracts, and various mucosal surfaces. Their collective contribution is instrumental in maintaining the overall health of the human host by actively participating in key processes like digestion, immune system regulation, and defense against harmful pathogens.

Demonstrating remarkable dynamism, the human microbiome exhibits substantial variability among individuals. Its formation commences at birth and undergoes continuous evolution throughout an individual's life, shaped by influences such as diet, environment, genetics, and medical interventions like antibiotics. Investigating the intricate interactions within the human microbiome has emerged as a prominent area of research, holding implications across diverse fields, including medicine, nutrition, and personalized healthcare.

In the early 1900s, pioneering scientists uncovered a groundbreaking revelation, recognizing the presence of an extensive community of diminutive living organisms collectively known as "microbiota" within the human body. These microorganisms, including bacteria, yeasts, and viruses, inhabit distinct regions such as the gut, skin, lungs, and oral cavity. Often termed as "the hidden organ," the human microbiota contributes more than 150 times the genetic information compared to the entire human genome, as supported by references. This discovery underscores the profound significance of comprehending the intricacies of the human microbiome.

II. The Human Microbiome: A Comprehensive Overview

Now, let's clarify a couple of terms: "microbiota" refers to the living microorganisms in a specific environment, like the oral or gut microbiota. On the other hand, "microbiome" is like the bigger picture – it includes the genomes of all the microorganisms, along with their structural elements, metabolites, and the surrounding conditions. So, microbiome is a broader term than microbiota.

In this review, we're focusing on understanding how microbiota impacts human health and diseases. The composition of microbiota varies from one place to another. The gut microbiota, for instance, is crucial for our well-being. It helps with food fermentation, guards against harmful pathogens, boosts our immune system, and even produces vitamins.

The gut microbiota is made up of different types, or phyla, with Firmicutes and Bacteroidetes being the major ones. Fungi (gut mycobiota), viruses, phages, and archaea also hang out there. Other than the gut, microbiota also exists in places like the oral cavity, lungs, vagina, and skin. The oral microbiota is the second-largest microbial community in humans, with various habitats like saliva, tongue, tooth surfaces, and gums.

Even though we used to think the lungs were sterile, recent studies show that they also have their own microbiota, including Actinobacteria, Bacteroidetes, Firmicutes, and Proteobacteria. Meanwhile, the skin's microbiota varies depending on the region, influenced by differences in glands and hair follicles. In general, Actinobacteria, Bacteroidetes, Cyanobacteria, Firmicutes, and Proteobacteria are common members of the skin microbiota. So, our body is like a bustling ecosystem with different microbial communities doing their thing in various places!

III. Role of the Microbiome in Maintaining Health

The evidence supporting the positive impact of the microbiome on overall health is multifaceted, particularly regarding the role of microbiota in the development of immune systems across various organs. This encompasses organs such as the gut, oral cavities, lungs, skin, and vagina, with a focus on elucidating interactions between human microbiota and both innate and adaptive immune responses. The innate immune response, facilitated by factors like secretory IgA, toll-like receptor 5 (TLR5), autophagy, and inflammasomes, plays a pivotal role in maintaining a homeostatic environment by eliminating pathogenic bacteria. Notably, dysbiosis of the microbiota can disrupt this delicate balance, adversely impacting the secretory IgA response and leading to unregulated bacterial growth.

Equally crucial is the adaptive immune response, which is integral to sustaining a healthy microbiota and immune equilibrium. This involves the differentiation and maturation of B and T cells, contributing significantly to immune tolerance to microbiota. The discussion extends to the impact of the gut microbiota on immune cells, underscoring the importance of microbiota development during the maturation of the immune system. Disorders in microbiota development are identified as potential contributors to compromised immunological tolerance and the onset of autoimmune diseases.

Additionally, the review sheds light on the maternal-neonatal microbial bond, particularly during birth and breastfeeding, emphasizing its influence on the establishment of the infant's immune system and microbiota. The text delves into the gut microbiota's role in promoting immune tolerance and its consequential impact on gut-associated lymphoid tissues, such as Peyer's patches. This comprehensive exploration underscores the intricate relationships between the microbiome and immune health, spanning various developmental stages and physiological processes.

IV. Influence of the Microbiome on Physiological Processes

Diet profoundly influences the gut microbiota, shaping its composition and metabolic activities. After birth, diet becomes a critical factor in shaping infant gut microbiota, adjusting to nutrient availability. Breast-fed infants show overgrowth of Actinobacteria and inhibition of Firmicutes and Proteobacteria, driven by breast milk oligosaccharides. Formula-fed infants exhibit an increase in Clostridia, Staphylococci, Bacteroides, and Enterobacteria. Throughout life, diet remains pivotal in organizing gut microbiota structure. Vegetarian diets, rich in fiber, promote the dominance of Firmicutes and Bacteroidetes, benefiting mucosal barrier integrity. Diets high in protein and fats correlate with an abundance of bile-tolerant species and metabolic diseases.

Age significantly influences gut microbiota composition. Early colonization is affected by the mode of delivery, with an increase in Proteobacteria followed by anaerobic strains. The first year of life is crucial for gut microbiota establishment, characterized by increased taxonomic diversity. In elderly individuals, a decline in microbial diversity, an increase in opportunistic pathogens, and decreased short-chain fatty acids (SCFAs) producing species are observed.

Host genetics play a substantial role in shaping the gut microbiota, with heritable taxa and functional categories showing similarities across mammalian species. Exercise positively correlates with gut microbiota diversity, enriching specific bacterial taxa and promoting SCFAs production. Antibiotic use disrupts gut microbiota, causing dysbiosis, and the effects depend on the type and duration of antibiotic treatment.

Smoking influences gastrointestinal and oral microbiota composition, with distinct changes observed in smokers compared to non-smokers. Geographical factors, encompassing lifestyle, genetics, and diet, impact the proportions of different phyla in human gut microbiota. Overall, understanding these factors is crucial for appreciating the intricate relationship between diet, lifestyle, and the gut microbiota in health and disease.

V. Disruptions in the Microbiome and Disease

The repercussions of changes in microbiota composition on various health conditions, including cardiovascular diseases (CVDs), cancer, respiratory diseases, diabetes, inflammatory bowel diseases (IBD), brain disorders, chronic kidney diseases, and liver diseases. The exploration of the microbiota's association with disease development underscores the profound influence of dysregulation in bodily functions attributed to external changes.

Within the segment dedicated to cardiovascular diseases, the article delves into the intricate linkages between oral and gut microbiota and conditions such as atherosclerosis and hypertension. Notably, it proposes that dysbiosis in oral microbiota, leading to periodontal diseases, is correlated with an elevated risk of CVDs.

The involvement of microbiota, particularly oral and respiratory microbiota, in cancer development. It highlights the association between dysbiosis of oral microbiota, as observed in conditions like periodontitis, and various cancers, including those affecting the oral, pancreatic, genitourinary, and gastrointestinal regions. Moreover, the article investigates the impact of respiratory microbiota, particularly in the context of lung cancer, emphasizing inflammation and immune modulation as potential pathways contributing to cancer development.

Emerging Trends and Future Directions

The intestinal microbiota significantly influences human health, and while some of its effects have been outlined in this review, many aspects are yet to be elucidated. Advancements in this research area emphasize the importance of cultivating representatives of the microbiota. Currently, only around 20% of intestinal microbes are identified as cultured organisms with known physiological functions. Cultivating the remaining majority is crucial, as it promises to unveil novel functions of this vast ecosystem. The optimism for new discoveries is bolstered by advancements in sequencing technologies and bioinformatics tools, enabling the study of an ecosystem comprising 100 trillion cells.

Certain inhabitants of the intestines perform metabolic conversions that extend beyond the digestive tract. For instance, Oxalobacter formigenes, a bacterium degrading oxalate, regulates oxalate concentrations in feces and urine, indirectly influencing the formation of kidney stones. This showcases the systemic impact of the microbiota on human physiology, suggesting that other intestinal constituents may similarly reveal unexpected functions. Recent research highlights a disrupted microbiota in autistic children, marked by an enriched abundance of Sutterella. While Sutterella is commonly found in the normal microbiota, its function remains unknown due to inactivity in classical microbiological tests. Future studies are essential to uncover the roles played by these (uncultured) microbiota constituents, providing a comprehensive understanding of the profound influence of the "forgotten organ" on human physiology.

CONCLUSION

This thorough review accentuates the pivotal role of the microbiome in shaping both human health and disease. Significant insights gleaned from research illuminate the intricate relationship between the myriad microorganisms that inhabit the human body and their involvement in various physiological processes. The microbiome emerges as a linchpin, actively contributing to fundamental functions such as digestion, nutrient absorption, and the modulation of the immune system, thereby playing a critical role in maintaining overall well-being.

Recognizing the significance of the microbiome for health and disease is of utmost importance. The review provides clarity on how microbial imbalances, referred to as dysbiosis, are intricately connected to a diverse range of health issues. Importantly, the impact of the microbiome extends beyond the confines of the gastrointestinal tract, exerting a systemic influence through complex interactions with the host.

The implications for clinical practice are substantial. Recognizing the microbiome's role opens new avenues for therapeutic interventions. Personalized medicine, targeting the microbiome to restore balance, emerges as a promising approach. The review underscores the need for healthcare professionals to incorporate microbiome assessments into diagnostic and treatment strategies, potentially revolutionizing disease management.

In conclusion, the review emphasizes that the microbiome is a key player in the complex tapestry of human health. A call to action resonates for intensified research efforts to unravel the intricacies of the microbiome-host relationship further. By

delving deeper into this dynamic ecosystem, we can unlock innovative therapies, paving the way for more effective treatments and preventive measures. Integrating microbiome knowledge into clinical practice stands as a transformative step towards enhancing patient outcomes and promoting a holistic approach to healthcare.

REFERENCES

1. Hou, K., Wu, Z. X., Chen, X. Y., Wang, J. Q., Zhang, D., Xiao, C., ... & Chen, Z. S. (2022). Microbiota in health and diseases. Signal Transduction and Targeted Therapy, 7(1), 1-28.
2. Rajili -Stojanovi , M. (2013). Function of the microbiota. Best practice & research Clinical gastroenterology, 27(1), 5-16.
3. Gomaa, E. Z. (2020). Human gut microbiota/microbiome in health and diseases: a review. Antonie Van Leeuwenhoek, 113(12), 2019-2040.
4. Senghor, B., Sokhna, C., Ruimy, R., & Lagier, J. C. (2018). Gut microbiota diversity according to dietary habits and geographical provenance. Human Microbiome Journal, 7, 1-9.