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HUMANS' MICROBIOME IMPACT ON DISEASE

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ABSTRACT

Hundreds of billions of microbes have coexisted with humans and now live on and within them. Microbial imbalance in the intestine is regulated by a variety of factors, and it has a strong link to human health and disease. The human microbiome is made up of bacteria, archaea, viruses, and eukaryotes that exist both within and outside our bodies. In both health and illness, these organisms have an impact on human physiology, promoting or inhibiting metabolic and immunological processes. Microorganisms colonise a wide range of sites on and inside the human body, adapting to the niche's particular properties. As a result of their biological interaction with the immune system throughout time, the indigenous organisms in the human body have become highly adapted to the immune system. The precise metabolic activities and functions of these microorganisms within each bodily location are accounted for by the inherent diversity of the human microbiota. As a result, it's critical to comprehend the human microbiome's microbial composition and behaviours as they relate to health and disease.

Keywords: Microbiome, Health, Infectious disease, Liver diseases, Human

I. INTRODUCTION

More than 100 trillion symbiotic microbes dwell on and within humans, playing a critical role in human health and disease. The human microbiota, particularly the gut microbiota, has even been dubbed a "essential organ" [1], as it contains almost 150 times more genes than the entire human genome [2]. The gut microbiota has been proven to play a role in basic human biological processes such as modifying metabolic phenotype, regulating epithelial development, and influencing innate immunity. [3], [4], [5], [6]. Chronic diseases such as obesity, inflammatory bowel disease (IBD), diabetes mellitus, metabolic syndrome, atherosclerosis, alcoholic liver disease (ALD), nonalcoholic fatty liver

disease (NAFLD), cirrhosis, and hepatocellular carcinoma have been associated with the human microbiota [7], [8] (Fig. 1).

A group of organisms dwelling and interacting with the human body is referred to as the human microbiota [1]. The interactions could be mutualistic, commensalistic, or pathogenic. The genetic content of organisms (microbiota) inhabiting a certain place in the human body is referred to as the human microbiome. Microorganisms colonise the skin, mucosa, gastrointestinal system, respiratory tract, urogenital tract, and mammary gland, among other anatomical body places. They develop a complex and distinct ecosystem that adapts to the niche's specific environmental requirements. [2]. The human body and its indigenous microbiota form a permanent bond (symbiosis) at birthing. These bonds are essential for maintaining general health and pleasure. Coevolution is how organisms create the microbiota; they actively adapt to their individual habitats and exist in their distinct niches within the human body [3–5]. As a result of their biological activities, these animals are identified as part of the body, resulting in a range of changes from conception to death. The human microbiome is constantly evolving in response to host conditions. Age, nutrition, lifestyle, hormonal swings, inherited genes, and underlying disease are all significant determinants of the human microbiome at any one time. Dysbiosis (a change in the makeup of the human microbiota) can, however, result in life-threatening illnesses [2]. A healthy microbiome has been shown to have an important role in overall health [2]. The human microbiome is primarily concentrated in the stomach. These organisms play an important part in human health maintenance and preservation. Changes in the immunological environment have been linked to a dysbiotic gut flora in previous studies on the human microbiome project. Also, life-threatening health conditions ranging from cancer, cardiovascular disease, bowel inflammatory disease and difficult-to-treat bacterial infections due to antibiotic resistance have also been linked with dysbiosis. [6, 7]. In general, this work aims to review and discuss the impact of the human microbiome on human disease and on maintaining health.

II. THE HUMAN MICROBIOTA IN HEALTH

The human microbiome has a significant impact on host physiology. Bacteria, archaea, viruses, and eukaryotic microorganisms are among the trillions of germs that inhabit the human body. The human body includes at least 1000 different types of bacteria and has 150 times the number of microbial genes as the human genome [2]. Microbiotic

composition and function vary depending on the host's region, age, gender, race, and diet. [27]. Commensal germs infiltrate the host soon after birth. This simple colony grows into a highly varied environment as the host matures [28]. Over time, host-bacterial partnerships have developed into mutually beneficial relationships. Symbiotic bacteria contribute to develop gut architecture by metabolising indigestible compounds, providing required nutrients, protecting against opportunistic pathogen colonisation, and metabolising indigestible substances. For example, the intestinal microbiota aids in the digestion of foods that are indigestible by the stomach and small intestine, as well as energy balanceDietary fibres like as xyloglucans, which are commonly found in vegetables and may be digested by Bacteroides species [30], make up the majority of these meals. Other non- digestible fibres, such as fructooligosaccharides and oligosaccharides, can be used by beneficial microbes such Lactobacillus and Bifidobacterium [31]. Research [32] has revealed the importance of the gut microbiota in lipid and protein homeostasis, as well as the microbial synthesis of essential nutritional vitamins. The usual gut microbiota produces short-chain fatty acids (SCFAs), such as acetic, propionic, and butyric acids, which serve as an energy source for the host intestinal epithelium [33]. These SCFAs have a range of activities in the gut, including motility regulation, inflammation, glucose homeostasis, and energy harvesting [34], [35]. In addition, the gut microbiota has been shown to transfer vitamins to the host, including folates, vitamin K, biotin, riboflavin (B2), cobalamin (B12), and possibly other B vitamins. According to a previous study [36], B12 can be produced from the precursor delta-aminolevulinate (ALA). Gut-colonizing bacteria also help the mucosal mucosa's humoral and cellular immune systems develop properly [37]. The innate immune system's hematopoietic and non-hematopoietic cells can detect and interpret microbial signals and metabolites into physiological responses [38]. GF mice have significant abnormalities in the development of gut- associated lymphoid tissue and antibody production, according to research comparing normal and GF mice [29], [39]. According to a study [40], the gut microbiota induces a tolerogenic response that operates on gut dendritic cells and suppresses the anti-inflammatory pathway of type 17 T-helper cells (Th17). Not all bacteria, however, are favourable to one's health. Some can cause inflammation in certain situations.

III. THE HUMAN MICROBIOTA IN DISEASE

A. The human microbiota and infectious diseases

Infection is one of the most common illnesses caused by dysbiosis of the microbiota. Infectious disease and its treatment have a big impact on the human microbiota, which determines how the disease presents in the human host (Fig. 2). Invading infections infect the intestinal mucosa, causing a large inflammatory response and subsequent intestinal bacterial translocation [41], [42]. Several studies have found a strong correlation between infection and microbiota dysbiosis, as well as the fact that infection is linked to viruses as well as the microbiome. [43], [44]. For example, patients with Clostridium difficile infection (CDI) have a dramatically changed intestinal microbiota [45], [46]. The progression of human immunodeficiency virus (HIV) [44], [47], hepatitis B virus (HBV) [48], and other disorders is also linked to disruption of the microbiota. [49], [50].

Maintenance of Homeostasis

The human microbiome is essential for the body's health and development (Figure 3). These organisms are responsible for launching the immune system in newborns and early children, as well as affecting inflammatory homeostasis and immunological regulation [73]. In a study published in 2015, Melli discovered that children who develop allergies later in life have a higher prevalence of Bacteroidaceae and anaerobic bacteria, as well as a lower concentration of Bifidobacterium adolescentis, Bifidobacterium bifidum, and Lactobacillus spp. [88]. Toxins removed from the bloodstream by renal filtration are stored in the bladder, providing substrates and an ideal environment for the urinary tract microbiota to deactivate dangerous chemicals [89]. In the aftermath of an infection, the actions of these organisms are interwoven. The protective system in the female vaginal tract is initiated by indigenous microbial flora, which is responsible for beginning innate immunity and secretions such as cytokines, antimicrobial peptides, and inhibitory chemicals. [97].

B. Development of Host Immune System

The immune system's ability to discern between dangerous pathogens and commensal organisms, which must be maintained through the co-evolution of indigenous microbiota and the immune system, establishes and reinforces immune responses [75]. The adaptive immune system's developmental characteristics are regulated by the microbiota in the stomach; hence, the mammalian immune system, which is responsible for regulating

microorganisms, is shaped by the human microbiota. Recent research into the functions of the human microbiome has revealed that a lack of these organisms or an early change in commensal organisms might lead to increased type II immunity and allergies due to abnormal immunological activity. A rise in incidence of childhood allergic rhinitis has been linked to changes in the microbiota induced by epigenetic impacts such as caesarean deliveries, a more sedentary lifestyle, pollution, and Western-style foods. Probiotics, breastfeeding, lifestyle changes such as allowing children to play outside in the early morning sun (to improve vitamin D production), and allergen specific immunotherapy have all been suggested as ways to help children's immune systems grow and avoid atopy [79]. The gut microbiota activates both proinflammatory (17cells) and regulatory T-cells (Tregs) in the intestine [77]. In addition, the human microbiome has a significant influence on innate immunity. The body's proinflammatory properties, for example, are diminished as neutrophils age These organisms exploit Toll-like receptor (TLR) and MyD88-mediated signalling pathways to drive neutrophil ageing. Microbial alterations drive older neutrophils to circulate less in models of sickle cell disease or endotoxin-induced septic shock, resulting in inflammation-related organ damage. As a result, these organisms actively regulate disease-promoting neutrophils, which are essential for inflammatory disease development. [97]. Furthermore, the intestinal microbiota helps in the defence against pathogenic organisms. They promote colonization resistance and the synthesis of antimicrobial compounds against invading pathogens. For example, a balanced gut microbiome may be responsible for regulating antibodies (CD8-T cells and CD4 cells) which respond to the invasion of influenza virus in the respiratory tract [79]. The gut microbiota also contributes to the improvement and maintenance of gastrointestinal functioning [95]. The intestinal immune system continues to struggle with the large concentration of organisms in the gut, since the immune system must accept commensal microbiota and food antigens while simultaneously keeping its ability to destroy infections. The development of immunological homeostasis depends on the activation of colonic regulatory T-cells (Tregs) [81]. Tregs are divided into two categories: thymus-derived and peripherally generated Tregs (pTregs). Although the distinction between these two immunological responses is difficult, they both play an important role in immune control. However, the pTregs, in specifically, needs microbiota to be active in the colon.

C. Host Nutrition

The colonic microbiota makes significant contributions to the nutritional requirements of their host [32]. Complex dietary elements that are indigestible (complex carbohydrates) are aggressively broken down by these organisms, making complex food ingredients readily available for absorption and assimilation. Short-chain fatty acids (SCFAs), which include acetic, propionic, and butyric acids, are significant end products of carbohydrates and amino acids in the digestive system. These three dietary components, when absorbed by the colonic mucosa, serve as energy sources and precursors for the synthesis of mucosal lipids, as well as stimulating epithelial cell proliferation, resulting in gut integrity maintenance. The synthesis of butyrate by the colonic microbiota from the fermentation of complex food ingredients protects the large bowel from cancer [76]. These critical microbial activities in the colon have resulted in the availability of key nutrients that are not readily available yet are necessary for colonic health [91]. In comparison to European newborns whose mothers consume Western diets low in SCFAs, African mothers and infants have been found to have a high level of Bacteriodetes and SCFAs in their faeces. Traditional and fermentable carbohydrate consumption has been linked to the prevalence of a healthy gut microbiome in studies. [79]. Another important function of the colonic microbiota is the provision of vitamins necessary for host development. Intestinal bacteria such as Bifidobacterium spp., Bacteroides spp., and enterobacteria are responsible for the production of vitamins [99]. Vitamin K, for instance, is an important coenzyme responsible for the synthesis of several clotting factors which include prothrombin (a deficiency of this leads to delayed blood clotting and excessive bleeding). Also, folic acid is an important precursor for DNA and RNA synthesis. Finally, they are involved in the synthesis of red and white blood cells [86]. Today, probiotics containing lactobacillus or Bifidobacterium are used in treatments of allergic diseases. Findings from the use of probiotics as treatment options have revealed that an enhanced immunomodulatory effect is achieved by reducing or inhibiting antigen-inducing T-cell activation and also suppressing cell signalling protein (tumour necrosis factor (TNF) involved in systemic inflammation [79].

VI. CONCLUSION

The proper and complete research of the human microbiome is necessary and this paper gives deep information of the connection between humans and microbiota. This paper gives better understanding and overview of whole research and useful into future study in optimizing all these organisms to fighting with life threatening diseases. It is very essential

that eh regular utilization of wide spectrum antibiotics may dislocate the human microbiota. This led to in instability or imbalance in the indigeneous microbial community making way for attack on pathogens. Nonetheless, care with the use of pre and probiotics ought to be improved. Therefore, several study should concentrated on the utilization of probiotic therapy in the medical care of the infectious disease. Additionally, future research should also highlight on the consequences of the human microbiome on mental health care and influences of mycobiome and the virome community on indigeneous microbiota as they perhaps contribute to dysbiosis.

VII. References

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