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**Review Article**

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# The Role of Lifestyle in Modulating the Gut Microbiome

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## ABSTRACT

The human gut, a dynamic and diverse ecosystem of trillions of microorganisms, plays an essential role in the host's health and disease. This review explores the influence of lifestyle choices like diet, stress, physical activity, and environmental factors on gut microbiome and their broader societal implications. Studies have reported that plant-based and Mediterranean diets enhance microbial diversity. At the same time, a sedentary lifestyle, chronic stress, processed foods, and alcohol consumption badly impact on the gut microbial composition and lead to many diseases like dysbiosis, obesity, and cardiovascular diseases. Geographic and ethnic factors also influence the gut microbiome. The consumption of fermented food and a diet high in fiber has a positive impact on the gut microbiome. The gut microbiome also has many societal implications, and the targeted intervention can help to reduce economic losses and public health costs and improve the overall health of everyone. This comprehensive review focuses on the links between lifestyle, gut microbiome, and societal well-being and suggests integrative strategies to promote sustainable health practices.

## INTRODUCTION

An abundant and diverse microbial community resides in the gastrointestinal tract of humans. Greater than 100 trillion microbes and about 2000 species have been reported within the intestine . Both pathogenic and symbiotic microorganisms are inhabitants of the human intestine, while around 1014 microbes reside in the colon of humans, making it one of the most populated habitats . More than 3 million genes are encoded by these microbes, which are known to produce a large number of bioactive compounds, and these compounds play a vital role in human health (Figure 1). Various beneficial activities have been reported in the gut microbiome for host health, like producing short-chain fatty acids and vitamins, immune homeostasis, digestion, and activity against pathogens. Alteration of gut microbiome badly affects human health and leads to diseases like type II diabetes, inflammatory bowel syndrome, and cardiovascular diseases . Short-chain fatty acids (SCFA) like propionate, butyrate, and propionate, produced by gut microbiome as a byproduct, are the primary energy source for epithelial cells of the intestine and strengthen the mucous layer. Studies on germ-free mice have shown that gut microbiome enhances the immunity of the intestine by affecting antigen-presenting cells, expression of toll-like receptors, lymphoid cells, and differentiated T cells and by altering systematic antibody expression and immunity via raised splenic CD4+ cells . Because of these facts about the gut microbiome, researchers are getting more interested in

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studying gut microorganisms. The gut microbiome changes quickly in response to the diet a person is consuming. For instance, if a person consumes a plant- or animal-based diet, the gut microbiome will change within 24h according to the diet .

The present study aimed to summarize the current knowledge on impact of lifestyle choices on gut microbiome and the implications of changes in gut microbial diversity because of lifestyle.

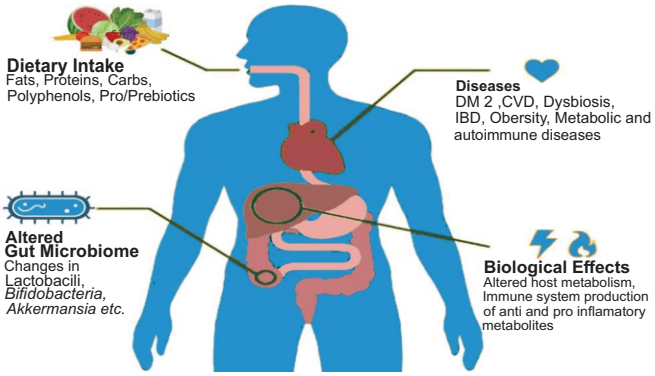


**Figure 1:** An Overview of Diet's Impact on Human Health, Diseases, and Gut Microbiome

There are many lifestyle choices that directly or indirectly influence the gut microbiome. Few of them are described below:

Geography and Ethnicity

Gut comparison analysis of individuals from European and African children's samples Lee *et al.*, reported that different countries gut microbiomes are not similar and have different compositions. They also compared the USA and Korean twin pairs fecal microbiota and found different gut microbiome compositions between the two countries. This study revealed that environmental factors and diet influence the gut microbiome. They further reported a massive difference in microbiota in families consuming different diets and environments while staying within the same country. A significant difference in the microbial composition of lean and obese patients was observed during their study in the USA and Korea. Fecal samples of 2084 persons from various ethnic groups residing in the same area were collected and analyzed for gut microbiome composition. The differences in the microbial composition indicate that ethnicity is one of the gut microbiota influencers Although other factors like person-specific genetic profile and some environmental factors might involve this variation, diet is the main contributor of gut microbial variation in these individuals. Rothschild *et al.*, reported a study in which they surveyed 1046 healthy persons sharing the same environment and belonging to different ancestors.Their analysis revealed that the person-specific genetic profile has a limited role in determining the composition of the gut microbiome. The impact of country of residence on gut microbial composition has been studied in individuals who migrated to the USA from Thailand. The individuals who emigrated from Thailand to the USA faced many challenges like obesity, metabolic diseases, and quick changes in gut microbial composition were observed among them. The gut microbiome changes observed in these individuals include loss of microbial diversity, native gut species loss, and *Bacteroidetes* increased in the place of *Prevotella* species with the passage of time.The reason for these changes can be a sedentary lifestyle, the adaptation of a Western diet, and food insecurity.

**Pet-Friendly Living**

Pet friendly life can be an environmental factor affecting gut microbial composition. Samples of 332 individuals living without and with pets were analyzed, and results showed no significant difference in microbial diversity. Still, the abundance of specific phyla, such as Firmicutes, was significantly higher.A link between the gut microbiome profile of infants and furry pets has been observed, with the abundance of *Oscillospira* and *Ruminococcus.* Both phyla are responsible for various allergies and obesity . As little literature is available on the relationship of pets and gut microbiome, more research must be conducted in this field.

**Physical Activity**

Regular physical activity/exercise plays an important role in the regulation of gut microbiome and its functionality. It can protect from the microbes associated with CVD and many other metabolic disorders.Therefore, physical exercise is a polypill for many chronic diseases/infections . Now, researchers are taking more interest in studying the impact of physical activity on the gut microbiome. They are looking for ways to improve physical health by modulating the gut microbiome, which can help fight microbial infections and various chronic diseases and delay aging with the help of gut microbiome.The relationships between microbiome, nutrition, and physical exercise have been focused on in adults and professional and non-professional athletes. Physical exercise can enhance microbial diversity, which is evidence of good health. But the problem is that persons with regular exercise or athletes use different kinds of diets and have entirely different routines for sex sports periodization and might depend on a particular sport. That's why their routine is different from that of the public. Therefore, the link between diet and gut microbial diversity in individuals who practice regular physical activity is strenuous to be established . A possible role of some gut microbial species has been established in physical activity. For instance, an increase in the

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abundance of *Prevotella copri* has been observed in the individuals following regular exercises.This bacterium plays a role in gene expression of genes involved in L-lysine metabolism. L-lysine is an amino acid not produced within our body and plays a role in muscular integrity '. Similarly, in a study, Scheiman *et al.*, reported an increase in *Veillonella atypica* in marathon runners. This bacterial species is known to play a role in muscle recovery by degrading lactate produced during physical activity . Likewise, in another study, Morita *et al.*, reported an increase in *Bacteroidetes uniformis* in male long-distance runners, enhancing their performance . These studies open new fields of opportunities to develop prebiotics, probiotics, and various symbiotic combinations to improve physical activities via food supplementation .

**Diet**

Diet plays a key role in maintaining optimal gut microbiome. The composition and functionality of gut microbes depend on dietary patterns and the availability of micro and macro-nutrients in the intestine. Several studies have been reported clinically and preclinically on the diet and stated that diet significantly influences the gut microbiome. The Western diet normally consists of simple sugars, and saturated fats tend to increase *Bacteroidetes* sp. This diet promotes bile-tolerant microbes like *Bacteroidetes* sp. and *Alistipes* sp. and tends to decrease *Firmicutes* sp. in the gut. Although main bacterial species remain dominant, a change in the diet influences the gut microbiome within 24h.Animal-based diets have less diverse gut microbiomes as compared to plant-based diets. The plant-based diet has high fiber levels, promoting the growth of fiber-fermenting bacteria. These fermenting microbes increase fermented products like short-chain fatty acids (SFA) and improve blood circulation in the gut. It is now an established fact that dietary interventions affect and change the gut microbiome, so changes in gut microbiome based on diet are not surprising anymore. For instance, the keto diet (KD) is known to influence the gut microbiome. Ma *et al.*, stated that there was an increase in the *Lactobacillus* and *A. muciniphila* population, and relative abundance was observed for *Turicibacter* and *Desulfovibrio* in individuals given a ketogenic diet.Both *Lactobacillus* and *A. muciniphila* are commensal bacterium known for SCA production.Many other studies have also reported a decrease in gut microbial diversity based on observed taxa and Shannon index among the persons given with KD. However, in a study, Swidsinski *et al.*, reported the change in gut microbiome based on KD if biphasic, indicating that it reduces the gut microbial diversity initially, but when a person receives KD diet for extended periods of time, then the microbial diversity increases automatically.However, gut diversity is not similar to that of individuals who have intermittent fasting compared to individuals with KD . Long-term dependency on the Mediterranean diet (MD) impacts on gut health. An increase in the concentration of *Prevotella, Prevotellaceae,* and *Bacteriodetes* and a decrease in *Lachnospiraceae* and *Firmicutes* has been observed in the individuals given Mediterranean diets . Furthermore, in the individuals who used to eat MD for a longer duration, an increase in the butyrate and propionate was observed. These SCFA were associated with higher microbial diversity when a comparison was established with the Western diet.The utilization of omega-3 fatty acids found in fish oil is associated with a higher level of docosahexaenoic acid (DHA) in the blood. This increased DHA level is associated with higher levels of *Ruminococcacae* and *Lachnospiraceae* bacterial families. These families are involved in the dietary fiber fermentation, resulting in the production of SCFAs in the human gut.Fecal metabolite N-carbamylglutamate can also be influenced by gut bacteria through dietary interventions.The microbial community shaping can be managed by the dietary intake of vitamins, minerals, micronutrients, and polyphenols.As gut microbial composition can be influenced by nutritional interventions, the gut microbiome can be modified easily by diet modification.Thus, a modified gut can achieve many physical and general health benefits (Table 1).

**Table 1:** Some of the gut microbes with associated diseases

| Bacteria | Key Characteristics | Linked Disease Conditions | Related Physiological Changes | References |
|---|---|---|---|---|
| *Akkermansia muciniphila* | Gram-negative, oval-shaped, nonmotile obligate anaerobe | Reduced presence in IBD, obesity, and psoriatic arthritis | Exhibits anti-inflammatory effects | [37] |
| *Escherichia coli* | Gram-negative, rod-shaped facultative anaerobe | Overabundance linked to IBD, UTIs, gastroenteritis, and meningitis | Activates TLR pathways | [38] |
| *Faecalibacterium prausnitzii* | Gram-positive, nonmotile, rod-shaped obligate anaerobe | Lower levels associated with IBD and obesity | SCFA production and anti-inflammatory properties | [39] |
| *Enterococcus sp* | Gram-positive, cocci-shaped facultative anaerobe | Includes pathogenic species causing UTIs, endocarditis, or bacteremia | Induction of anti-inflammatory response | [40] |
| *Eubacterium sp* | Gram-positive, rod-shaped obligate anaerobe | Reduced presence linked to IBD | Produces SCFAs and beneficial phenolic acids | [41] |
| Roseburia sp | Gram-variable, curved, motile obligate anaerobe | Decreased levels noted in IBD | SCFA production | [42] |

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|---|---|---|---|---|
| *Clostridium* sp | Gram-positive, rod-shaped obligate anaerobe; spore-forming | Associated with diseases like tetanus, botulism, gas gangrene, and pseudomembranous colitis | Supports TH17 cell generation | [43] |
| *Bilophila* sp | Gram-negative, obligate anaerobe; urease-positive, bile-resistant, catalase-positive | B. wadsworthia linked to colitis, liver abscesses,gangrenous appendicitis, cholecystitis, FG, empyema, and HS | Stimulates pro-inflammatory TH1 immune response | [44] |
| *Alistipes* sp | Gram-negative, rod-shaped obligate anaerobe; bile-resistant, pigment-producing | Found in cases of acute appendicitis, brain abscesses, and perirectal abscesses | contribute to the production of beneficial metabolites | [45] |
| *Bacteroides* sp | Gram-negative, rod-shaped obligate anaerobe; variable motility | Higher abundance linked to IBD | Activates CD4+ T cells | [46] |
| *Lactobacillus* sp | Gram-positive, rod-shaped facultative anaerobe | Contributes to reducing IBD | SCFA synthesis exhibits anti-inflammatory and anti-cancer properties | [47] |
| *Bifidobacterium* sp | Gram-positive, branched, nonmotile obligate anaerobe | Lower levels observed in obesity | Produces SCFAs, enhances gut mucosal barrier, reduces intestinal LPS | [48] |

**Stress**

Gut dysbiosis is often associated with stress, indicating that the gut microbiome also responds to chronic stress. A study on germ-free mice showed the production of adrenocorticotropic hormone (ACTH) and corticosterone compared to the control when mild stress was given to the mice. This indicates that the gut microbiome responds to stress and is critical in hypothalamic pituitary adrenal(HPA) axis development. The gut microbiome is also associated with behavioral and physiological changes in response to exposure to stress, like HPA axis dysregulation, social and behavioral changes, impaired cognition, and intestinal barrier function, causing intestinal permeability, which leads to leaking gut and increased inflammation. Now, it is established that stress badly impacts the gut microbiome, damages the microbial community's ecology, and promotes dysbiosis. Many clinical and animal-based studies have reported that stress negatively impacts gut health. Various kinds of stresses like restraint conditions, maternal separation, crowding, heat stress, and noise were able to negatively change the gut microbiome in different animal model studies. For instance, chronic restraint and maternal separation stress tend to lower the *Lactobacillus* level. A survey of the animal model, which was kept under stress, showed improved cognition, behavioral, and biochemical results after administering *Lactobacillus*. Under chronic stress conditions, a decrease in the Bacteriodetes abundance and an increase in the clostridiales family has been observed. Both of these correlate with changed pro-inflammatory cytokines levels .All these studies indicate that stress directly impacts the gut microbiome, which may be associated with various diseases like dysbiosis. So, stress management techniques must be adopted in our daily life to maintain gut microbiome at optimal conditions.

**Prebiotics**

Prebiotics, from the family of dietary fibers, play a significant role in the gut microbiome. Prebiotics can be defined as substrates that can be utilized by host microorganisms that have health benefits for the host system.The most common prebiotics are HMOs, FOS, galacto-oligosaccharides, and inulin. These prebiotics promote the growth of probiotic bacteria like *Lactobacilli* and *Bifidobacteria*. These probiotic microbes produce SCFA and many other bioactive compounds that have health benefits for the host system . Many studies have already reported that prebiotics can influence the ability of gut microbes to produce SCFAs. The SCFAs activate the GPR43/41 receptors of the L cells, thus promoting the secretions of PYY and GLP-1. They also promote the secretions of the BLP-2. This peptide maintains the gut barrier functions by stimulating blood flow, stimulating proliferative epithelial cells of the intestine, and improving the integrity of tight junctions . After all, the prebiotic and gut microbic interactions play a role in the reduction of intestinal permeability, and they also decrease food intake, prevent metabolic endotoxemia and hepatic steatosis, and improve sensitivity and secretions of insulin. All of these are known to reduce inflammation(Figure 2).

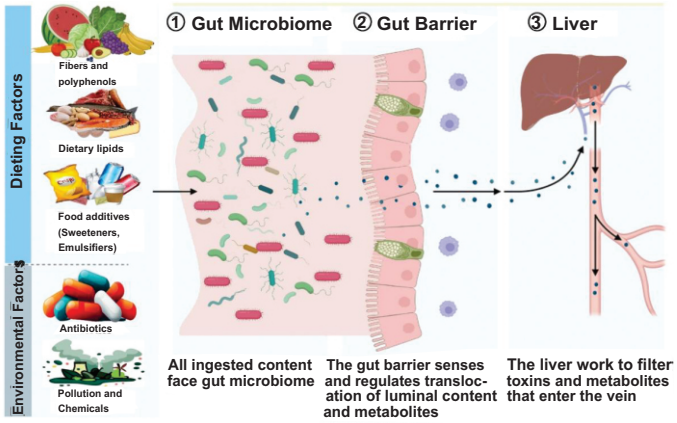


**Figure 2:** There Are Three Lines of Defense. (1) Gut Microbiome Influenced by Environmental Factors and Diet. (2) Then They Interact with Gut Barrier and The Gut Barrier Regulate the Translocation of Metabolites and Luminal Components. (3) The Liver Work to Filter The Toxins and Metabolites.

**Polyphenols**

Polyphenols abundantly found in plant-based diets, including tea, fruits, coffee, vegetables, and wine, are the

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most complex metabolic compounds.They are divided into two main groups: non-flavonoids and flavonoids. Flavonoids are divided into flavanols, anthocyanins, isoflavones, and flavanones. At the same time, non-flavonoids are divided into lignans, stilbenes, and phenolic acids. Polyphenols are not present in blood circulation because most of them are found in food as polymers, glycosides, and esters that may not be absorbed in their native form, so most of them work locally. Polyphenols have been considered for their ability to prevent different diseases that may be caused by oxidative stress, and they are also known for their potent antioxidant potential. Gut microbes are known for their ability to produce various enzymes that enhance the bioactivity and bioavailability of polyphenols in the intestine. So, the polyphenols affect the gut microbiome composition. The polyphenols strengthen the growth of gut microbes like *Bifidobacterium*, *Lactobacillus*, A. *muciniphila, Faecalibacterium*, and *Roseburia* and inhibit the growth of pathogenic microorganisms.The gut microbiota and polyphenols interaction also play a role in the gut barrier function anticarcinogenic and anti-inflammatory effects. Phenyl propionic acid, a phenolic compound produced by the gut microbiome, has anti-inflammatory activity and plays a role in the gut barrier using the dependent mechanism of aryl hydrocarbon receptor(AhR) . The polyphenolic compounds 4-hydroxyphenylacetic acid and Hydroxyphenylacetic acid have been known for their antioxidant and anti-inflammatory potential and protect the body from obesity, cardiovascular disease, and many types of cancers . Many other phenolic acid compounds, like gallic acid, ferulic acid, and caffeic acid, are produced by gut microbes using dietary polyphenols and have many health benefits.

**Fatty Acids**

The function and composition of the gut microbiome are also greatly influenced by the dietary fat that any individual is consuming. For example, saturated fatty acids, usually present in processed food and animal fat, increase pro-inflammatory microbes and decrease gut microbial diversity . Polyunsaturated fatty acids(PUFAs), like omega-3, usually present in flaxseed and fish oil, are known to enhance the growth of A. mucinipila and Bifidobacterium, which play a role in health improvement .Some gut microbes, like Clostridium, *Lactobacillus, Enterobacter,* and *Bifidobacterium,* can metabolize PUFAs into keto and hydroxy derivatives. The beneficial effect of HYA and CLA has been reported in the mice model of cancer, obesity, and colitis by activating PPARa, GPR140, PPARy, and GPR120 and using peristalsis via EP3 activation .Dietary cholesterol is highly dependent on gut microbiome composition. Some cholesterol is absorbed in the upper portion of the intestine, and about 2g of cholestrol enters the colon daily. In the colon, cholesterol-degrading bacteria convert the cholesterol to coprostanol and then, to a lesser extent, form the coprostanone.Some cholesterol-degrading microbes, such as *Oscillibacter* and *Dysosmobacter,* have been cultured and isolated, but overall, isolating cholesterol-degrading bacterial species is a complicated and challenging task. These microbes have shown activities to lower the cholestrol level in humans and have demonstrated the potential to convert cholesterol to comprostanone .

**Artificial Sweeteners**

Many non-calorie artificial sweeteners are used to enhance the quality and taste of packaged foods. Although food regulatory authorities approve of them, many of the artificial sweeteners are known to cause risks for various diseases. In research studies, aspartame, sucralose, and saccharin have been reported to cause greater glucose intolerance than glucose. Saccharin has more potential to cause glucose intolerance than other ones. Most of the non-caloric artificial sweeteners pass the digestive tract while remaining undigested. These undigested artificial sweeteners interact with the gut microbiome, changing their function and composition. Artificial sweeteners may also cause type 2 diabetes by upregulating the pathways involved in LPS biosynthesis, as revealed by metagenomic studies . A positive correlation between metabolic indicators like blood glucose levels and hemoglobin A1c and artificial sweetener consumption in humans has been reported. Regular usage of artificial sweeteners and refined sugar badly impacts the gut microbiome composition. This altered composition may lead to metabolic disorders like diabetes, impaired glucose metabolism, reduced microbial diversity, and gut microbiota deviation .

**Emulsifiers**

The emulsifiers are typically used to improve the shelf life and texture of food, but they also have a terrible impact on gut barrier function and gut microbiota. Although they are widely used in the food industry, safety concerns about emulsifiers still need to be resolved. The emulsifiers like polysorbate 80 and carboxymethylcellulose have been reported to induce many metabolic diseases. They mutate the intestinal mucus layer and thus lead to leaking gut by increasing gut permeability. Some emulsifiers like carboxymethylcellulose disturber the gut microbial community by overgrowth of some bacterial species while many like polysorbate 80, play a role in microbial translocation.These emulsifiers have also been reported to cause metabolic syndrome and inflammation in mice models. Furthermore, these emulsifiers damage the

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mucus layer, making direct contact between intestinal walls and bacterial cells and leading to pathogenic infections.

**Alcohol**

Alcohol is also known to cause changes in the gut microbiome. In alcohol-addicted individuals, the gut microorganisms play a role in alcoholic liver disease, and dysbiosis is commonly observed in alcoholic individuals. In patients suffering from alcoholic liver diseases, the abundance of *Enterococcus* and *Bacteroidetes* has been observed. A study conducted on mice models has reported overgrowth of some bacterial species, like Enterobacteriaceae class. The study further reported the occurrence of intestinal inflammation upon regular alcohol consumption for seven days.The change in gut microbiome composition upon alcohol consumption does not seem to be influenced by ethanol: acetate production, but by the enzymes that the host produces also play a role. Some studies have suggested that probiotics may help improve liver-associated enzyme levels, which are affected by alcohol consumption .

**Cigarettes**

Studies on e-cigarettes and cigarettes have reported that smoking contributes to low gut microbial diversity. They also reported that this leads to an imbalance between gut microbial species. The exact mechanisms that lead to low gut microbial diversity are unknown, but most likely many of the toxic chemicals in the cigarette might be responsible. Many of the compounds like aldehydes, benzenes, heavy metals, nitrosamines, and polycyclic aromatic hydrocarbons may change the pH of the gut, affect the production of organic acid, and might act as antimicrobial agents for the gut microbiome, and can be metabolized by gut microbiome to produce further toxic substances. These compounds might inhibit some microbes' growth and promote others' development, thus leading to a dysbiosis state.Nicotine, a chemical compound found in cigarettes, damages the gut microbial community by reducing the growth of *Firmicutes* and Actinobacteria while promoting the growth of *Bacteroidetes* and *Proteobacteria.*

**Environmental Pollutants**

Environmental pollutants like pesticides, dyes, and heavy metals have been reported to affect the gut microbial composition, leading to harmful health effects and dysbiosis.For instance, exposure of mice to arsenic, cadmium, and lead heavy metals causes damage to the gut microbial structure and relative abundance by altering ratios of *Bacteroidetes* and *Firmicutes*.In response to heavy metals, gut microbes offer physical barriers to the heavy metal absorption and secret enzymes that detoxify heavy metals and convert them to less toxic substances. Probiotics like *Bifidobacterium* and *Lactobacillus,* usually present in fermented food products, can detoxify heavy metals, limit their absorption, reduce the expression of metal transporters, and maintain gut barrier integrity . Pesticides like fungicides, insecticides, and herbicides also affect the gut microbiome by promoting some microbes' growth while inhibiting others' growth. Still, sometimes they also show contrasting results . More research should be conducted on the impact of pesticides on the gut microbiome to understand the exact role of these compounds on gut health.

**Sleep and Circadian Rhythm**

The gut-brain axis not only plays a role in mental health disorders but also contributes to the sleep cycle. The immune system, vagus nerve, serotogenic system, and microbial metabolites are all communicating vehicles between the brain and gut, which regulate the sleep cycle". Recently, studies have reported a rhythm in the gut microbiome and its metabolites that might be controlled by feeding patterns and circadian cues, *i.e.*, light/dark cycles . Host circadian rhythm patterns influence the gut microbiome, and gut microbes produce metabolites to modulate host rhythm.An equilibrium disturbance like traveling has been associated with gut microbiome changes. These changes might be caused by sleep loss and lag, which affect the diurnal rhythms and result in the shift in function and composition of gut microbes . The state of dysbiosis has been observed in individuals having disturbed sleeping cycles. Dietary supplements like vitamins, probiotic intake, attention to feeding habits can potentially improve gut microbiome, sleeping cycle, and circadian rhythm . All these indicate that the sleep cycle and circadian rhythm influence the gut microbiome, which results in various health consequences.

## CONCLUSIONS

The gut microbiome plays an essential role in disease prevention and promotes the individual's overall health. This review article focused on the multifaceted impact of lifestyle choices like physical activity, stress, diet, and environmental factors on gut microbial diversity and functionality. The gut microbiome helps fight against chronic disease and improves mental health via the gut-brain axis. The targeted interventions for gut microbiome can significantly enhance health outcomes. Beyond individual health benefits, the societal effects of gut microbiome modulation are profound. A healthy gut can help us eliminate the economic burdens of healthcare systems. Using a plant-based and fiber-containing diet can improve gut health, which can solve many health problems worldwide, especially in underdeveloped areas. The fiber-rich diet, physical activities and sustainable practices

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benefit physical fitness and boost the gut microbiome. Advanced research and emerging technologies provide an opportunity to address many gut issues and quick tests to diagnose gut problems. These technologies can help to provide personalized gut health interventions and enable precise and practical strategies to improve public health.

## Authors Contribution

Conceptualization: NM
Methodology: AS, AA, SHAS, HJ, WA, ZN, RM, HRK
Formal analysis: AS, AA, SHAS, HJ, WA, ZN, RM, HRK
Writing, review and editing: NM, IL

All authors have read and agreed to the published version of the manuscript.

## Conflicts of Interest

All the authors declare no conflict of interest.

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