MEDVIX PUBLICATIONS

Journal of Medicine Care and Health Review
Research Article | Open Access | ISSN 3065-1719 | Volume 01 | Issue 04

Effects of Ultra-Processed Food on Human Gut Microbiota

Krishna K.Joshi[1*], **Jinesh P. Kaneriya**[2], **P D Gupta**[3]

[1,2]Atmiya University, Rajkot.

[3]CCMB, Hyderabad, India.

Received date: 11 October 2024; **Accepted date:** 28 October 2024; **Published date:** 02 November 2024

Corresponding Author: Krishna K. Joshi, Atmiya University, Rajkot.

Citation: Krishna K. Joshi, Jinesh P. Kaneriya, P D Gupta. Effects of Ultra-Processed Food on Human Gut Microbiota. Journal of Medicine Care and Health Review 1(4). https://doi.org/10.61615/JMCHR/2024/NOV027141102

Abstract

Food is one of the essential items for the sustenance of life. The food that we eat is also the food for the organisms (microbiota) that live in our intestines. Like us microbiota also has food preferences. It is now well established that several body functions are regulated by the microbiota, and therefore it is essential to provide them with food of their liking. Healthy gut microbiota prefer foods rich in Fiber such as fruits, vegetables, whole grains, and legumes. Fiber acts as a prebiotic, which nourishes the beneficial oral and gut microbes. Some foods to avoid for a healthy gut include red and processed meat products together with refined sugar and grains and fried foods. These have a negative impact on diet quality.

Introduction

Due to the Industrial Revolution, people preferred ready-to-use packed foods, fast foods, and ultra-processed foods (UPF).**[1]** Globally, food systems have changed instead home home-cooked food people prefer ready-to-eat food. Advancements in food processing technologies were developed which facilitated the large-scale production of key cooking ingredients, including oils, fats, sugars, flour, and salt. By the mid-20th century, these industrial processing techniques had evolved to produce a diverse array of food products that ensured microbiological safety, extended shelf life, and offered convenience for the consumption of food across various social contexts **[2]**. Techniques such as roller milling, pressure rendering, and extrusion, along with chemical processes like hydrogenation and hydroxylation, were developed. The incorporation of artificial flavors, preservatives, and other additives further enhanced the functionality and appeal of these products. These technological innovations enabled the mass production of processed foods, which became widely available and affordable throughout high-income countries. The ability to produce food products year-round with minimal preparation time has increasingly aligned with the values and lifestyles of high-income societies, where convenience and time efficiency have become highly prioritized over the past few decades.

This dietary pattern is marked by the dominance of energy-dense but nutrient-poor foods, including fast foods and pre-packaged food items, which contribute significantly to daily caloric intake **[3]**. The convenience of these pre-packaged foods offering reduced cooking time, cost-effectiveness, and enjoyable consumption makes them a staple in many diets. However, the Western diet, combined with an inactive lifestyle, is linked to chronic metabolic inflammation, which is believed to play a role in the development of various prevalent non-communicable diseases, such as obesity, diabetes, cardiovascular disease, gastrointestinal, and cancer **[4]**. Research into the health impacts of ultra-processed foods (UPFs). UPFs constitute a major component of this dietary pattern. There is increasing evidence that UPFs contribute to rising rates of non-communicable diseases, morbidity, and mortality through several mechanisms **[5]**. The production of highly processed foods worldwide coincided with a notable increase in the prevalence of chronic inflammatory diseases, including metabolic syndrome and inflammatory bowel disease (IBD) **[6]**. This observed relationship has prompted extensive scientific inquiry into the potential association between the consumption of highly processed foods and the risk of chronic diseases. In this review, we evaluate the predominant classification systems for processed foods and examine with particular emphasis the role of the intestinal microbiota.

UPFs Definition and Classification

UPFs are characterized by their high degree of processing, low nutritional quality, and the presence of numerous non-nutritive additives and high sugar, salt, and fat content. The classification of foods, including UPFs, can be systematically organized based on their level of processing. One widely accepted framework is the NOVA classification system, which categorizes foods into four groups **[7]**

1. Unprocessed or Minimally Processed Foods: These foods are either consumed in their natural state or undergo minimal processing such as washing, drying, boiling, or pasteurization. Examples include fresh fruits, vegetables, meat, milk, and eggs etc.
2. Processed Culinary Ingredients: These are substances extracted from foods or plants and used in cooking to enhance flavor or preserve foods. They include items such as sugar, salt, oil, and vinegar, etc.
3. Processed Foods: This category includes foods that have been processed with the addition of ingredients such as sugar, salt, or oil but still retain

most of their original characteristics. Examples include canned vegetables, cheese, and bread, etc.

4. Ultra-Processed Foods (UPFs): UPFs are industrial formulations typically consisting of substances extracted from foods or synthesized in laboratories. They often contain multiple added ingredients, including artificial additives, preservatives, colorings, flavorings, and emulsifiers, refined ingredients high-fructose corn syrup, hydrogenated fats, refined flours, synthetic compounds artificial sweeteners, and flavor enhancers **[8]**.

Examples of UPFs include sugary drinks, packaged snacks, instant noodles, and ready-to-eat meals etc. Ultra-processed foods (UPFs) are foods that have been significantly altered from their original form through the use of industrial processing and the addition of various ingredients. These ingredients can include additives, preservatives, flavorings, and emulsifiers, among others**[9]**.

Table 1. Common components used in making UPFs

Component	Function	Examples
Sweeteners	Add sweetness, often without calories or with reduced calories	High fructose corn syrup, aspartame, sucralose
Preservatives	Extend shelf life and prevent spoilage	Sodium benzoate, potassium sorbate
Colorants	Enhance or modify the color of the food	Red 40, Yellow 5
Flavorings	Add or enhance flavors	Artificial vanilla flavor, smoke flavoring
Emulsifiers	Improve texture and stability, prevent separation	Lecithin, mono- and diglycerides
Stabilizers	Maintain consistency and prevent separation	Guar gum, xanthan gum
Thickeners	Increase viscosity and improve texture	Pectin, gelatin
Acidity Regulators	Adjust or control the pH level	Citric acid, sodium citrate
Anti-oxidants	Prevent oxidation and rancidity	BHT (butylated hydroxytoluene), vitamin E
Artificial Flavors	Provide specific flavors not naturally present	Ethyl maltol, isoamyl acetate
Artificial Colors	Provide or enhance color	Tartrazine, carmine
Fortifiers	Add nutrients that are not naturally present	Calcium carbonate, vitamin D
Texturizers	Modify the texture to mimic natural textures	Hydroxypropyl cellulose, modified starches
Reinforcements	Enhance nutritional content or other properties	Protein isolates, fiber supplements
Stabilizing Agents	Maintain product consistency over time	Sodium alginate, carrageenan

Importance of gut Microbiota in human health and disease

The gut microbiota refers to the complex and diverse community of microorganisms, including bacteria, viruses, fungi, and archaea, residing in the gastrointestinal (GI) tract. This microbial ecosystem plays a critical role in maintaining overall health, influencing various physiological processes, and interacting with the host's immune system **[10]**. The gut microbiota is highly diverse and varies between individuals based on factors such as age, diet, genetics, and environment. The gut microbiota is predominantly composed of bacterial species from major phyla such as *Firmicutes*, *Bacteroidetes*, *Actinobacteria, and Proteobacteria*, *cynobacteria*, *Verrucomicrobia* healthy gut microbiota is characterized by a high degree of microbial diversity,**[11]**. Which is thought to contribute to resilience against disease and disturbances. The gut microbiota is a vital component of human health, contributing to digestion, metabolism, immune function, and overall well-being **[12]**. Understanding its complex interactions with the host and the impact of external factors such as diet and lifestyle is crucial for developing strategies to maintain or restore a healthy microbiota and prevent or manage chronic diseases. The gut microbiota performs numerous essential functions that contribute to host health. Microbes help digest complex carbohydrates, ferment dietary fibers, and produce short-chain fatty acids (SCFAs) like acetate, propionate, and butyrate, which provide energy and support gut health**[13]**. Certain gut bacteria synthesize essential vitamins, such as vitamin K and some B vitamins, which are crucial for various metabolic processes**[14]**. The gut microbiota interacts with the immune system, helping to regulate immune responses and maintain a balanced immune environment. It plays a role in the development of immune tolerance and protection against pathogens. The gut microbiota helps maintain the integrity of the intestinal barrier, preventing the entry of harmful substances and pathogens into the bloodstream. The metabolism of dietary components by gut microbes results in the production of metabolites that can influence host physiology, including SCFAs that affect inflammation and metabolism**[15]**. Microbial interactions with the gut-associated lymphoid tissue (GALT) play a critical role in shaping immune responses and preventing autoimmune and inflammatory

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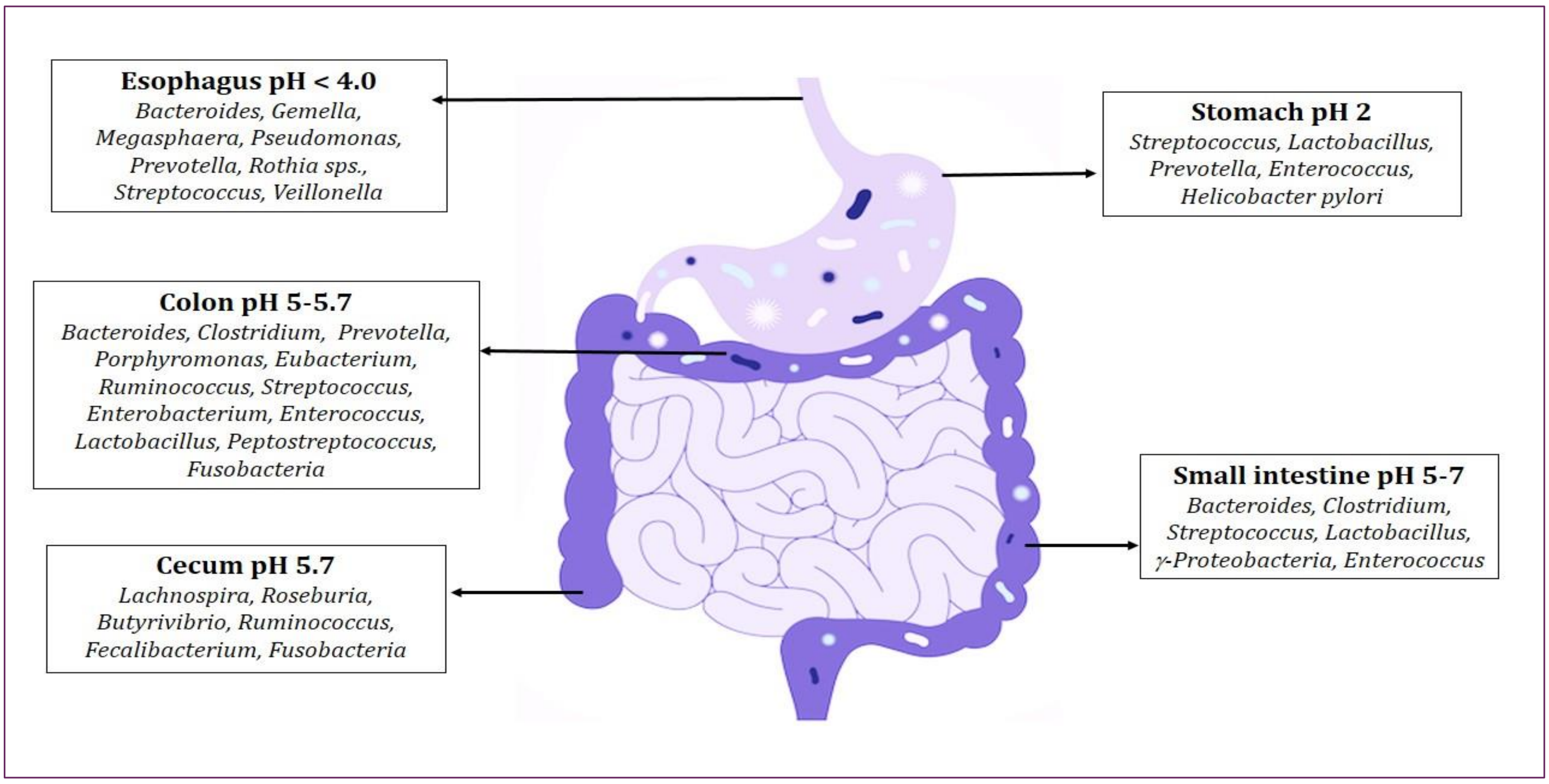
conditions. Gut microbes communicate with host cells through various signaling pathways, influencing gut motility, mood, and overall health. Diet and lifestyle factors have a profound impact on the composition and function of the gut microbiota. The intake of fiber-rich foods promotes beneficial microbial growth and diversity, while high consumption of processed foods and antibiotics can disrupt the microbial balance. Physical activity, stress, and sleep patterns can also affect the gut microbiota. The imbalance in the gut microbiota has been linked to a range of health conditions, including metabolic syndrome, inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), and even mental health disorders like depression and anxiety. Modulating the gut microbiota through dietary changes, probiotics, and fecal microbiota transplantation is being explored as potential therapeutic strategies for various health conditions **[16]**.

The gut microbiota's makeup differs depending on the digestive tract's location. These microbes work together to maintain a balanced gut environment, support digestion, and contribute to overall health. The gut microbiome is highly diverse, and the specific composition can vary from person to person based on diet, lifestyle, and other factors **[17]**.

Table 2. Outlining some beneficial microbes commonly found in the human gut, along with their general functions

Microbe	Genus	Function
Lactobacillus acidophilus	Lactobacillus	Helps digest lactose, produces lactic acid, and maintains a healthy pH balance.
Bifidobacterium bifidum	Bifidobacterium	Supports immune function, helps with digestion, and maintains gut barrier integrity.
Bacteroidesthetaiotaomicron	Bacteroides	Aids in the breakdown of complex carbohydrates and contributes to the synthesis of vitamins.
Faecalibacteriumprausnitzii	Faecalibacterium	Produces butyrate, which is important for colon health and has anti-inflammatory effects.
Ruminococcusbromii	Ruminococcus	Helps digest resistant starches and contributes to overall gut health.
Akkermansiamuciniphila	Akkermansia	Promotes mucin production, which supports the intestinal barrier and may help with metabolic health.
Eubacteriumrectale	Eubacterium	Contributes to butyrate production, which is beneficial for gut health and inflammation.
Enterococcus faecium	Enterococcus	Supports gut health by preventing the growth of harmful bacteria and contributing to a balanced microbiota.
Lactobacillus reuteri	Lactobacillus	Produces antimicrobial substances, helps in digestion, and has been linked to reduced gastrointestinal infections.
Prevotellacopri	Prevotella	Assists in the breakdown of dietary fibers and may influence immune responses.

Fig: Distribution of the normal human gut microbial flora.



Rational Study of UPFs

The rationale for studying ultra-processed foods is multifaceted, encompassing the need to understand their health impacts, inform dietary guidelines and policies, address social and economic factors, advance food science, enhance public awareness, and contribute to broader health research. Such studies are essential for developing effective strategies to mitigate health risks associated with UPFs and promote healthier eating habits, ultimately improving public health outcomes. Ultra-processed foods (UPFs) can influence several metabolic pathways in humans due to their specific nutrient composition, additives, and processing methods. Below is a table outlining the key metabolic pathways affected. Ultra-processed foods can

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influence several metabolic pathways in humans due to their specific nutrient composition, additives, and processing methods.UPFs typically contain high levels of sugars, unhealthy fats, and artificial additives, and lack dietary fiber, which is crucial for nourishing beneficial gut bacteria this can affect the overall microbial composition in the gut Some intestinal microbes,**[18]**particularly certain bacteria and yeasts can ferment available carbohydrates in UPFs. This process breaks down complex carbohydrates and sugars into simpler compounds, producing gases (CO_2 and CH_4) and short-chain fatty acids (SCFAs) as byproducts **[19]** this product cannot be digested easily by intestinal microbes and enzymes so it interferes with the digestion process and metabolic pathway in the gut,**[20]** table outlining the key metabolic pathways affected by UPFs.

Table 3. UPFs affect metabolic pathways along with the mechanisms and potential health impacts

Metabolic Pathway	**Influenced By**	**Mechanism of Effect**	**Health Impact**
Glycolysis	High sugar content	Increased glucose availability leads to enhanced glycolysis.	Can contribute to insulin resistance and type 2 diabetes.
Lipogenesis	High-fat content, particularly saturated and trans fats	UPFs can stimulate fat synthesis and storage.	May lead to obesity, dyslipidemia, and cardiovascular diseases.
Fatty Acid Oxidation	High intake of unhealthy fats	Reduced fatty acid oxidation due to excess fat storage.	Impaired fat metabolism, contributes to obesity and metabolic syndrome.
Short-Chain Fatty Acid (SCFA) Production	Low fiber content	Reduced fiber fermentation by gut bacteria limits SCFA production.	Lower SCFA levels can impair gut health and increase inflammation.
Gut Microbiota Metabolism	Additives (e.g., emulsifiers, artificial sweeteners)	Altered microbial composition affects metabolism and by-products.	Dysbiosis, increased inflammation, and metabolic disturbances.
Inflammatory Pathways	High levels of added sugars, fats, and additives	UPFs can increase production of inflammatory cytokines and disrupt gut barrier function.	Chronic inflammation linked to diseases like obesity, cardiovascular disease, and type 2 diabetes.
Detoxification Pathways	Preservatives and artificial additives	UPFs may affect liver function and detoxification processes.	Increased toxic burden and potential liver stress.
Insulin Signaling Pathway	High glycemic index foods, high added sugar content	Frequent insulin spikes due to rapid glucose absorption.	Insulin resistance and increased risk of type 2 diabetes.
Cholesterol Metabolism	High intake of trans fats and processed oils	Disruption in cholesterol synthesis and regulation.	Increased LDL cholesterol and risk of atherosclerosis.
Appetite Regulation	High sugar and fat content	Disruption of hormones like leptin and ghrelin that regulate hunger and satiety.	Increased appetite, overeating, and weight gain.
Energy Homeostasis	Imbalance in calorie intake vs. expenditure	UPFs often provide high-calorie content with low satiety.	Disruption in energy balance, leading to weight gain and obesity.

Gut microbiota in human disorder

The gut microbiota plays a significant role in various disorders associated with the consumption of ultra-processed foods. The classification of microbiota related to these disorders highlights specific taxa that exhibit alterations in response to UPF consumption, contributing to conditions alterations in gastrointestinal microbiota that have been linked to several major human diseases, including obesity, diabetes, cardiovascular diseases, cancer, hypertension, and inflammatory bowel diseases (IBDs)**[21]**. Understanding these associations can aid in the development of targeted dietary interventions and therapeutic strategies. Several studies using epidemiological, physiological-based approaches, along with experiments, have the significant role of intestinal microbiota in both health and disease **[21]**. The term "dysbiosis" refers to changes in the composition of gut microbiota that are often observed in various diseases, **[22]**. Defining a healthy microbiome composition remains challenging due to significant inter-individual variability **[23]**. A balanced gut microbial community is crucial for establishing a mutually beneficial relationship between the host and its microbiome.

1. Obesity

Recent alterations in gut microbiota composition have been identified as significant factors in the development of obesity [24]. Certain gut microbiota species, often referred to as "obesogenic gut microbiota," include Firmicutes, Bacteroidetes, Rhizobium, Lactococcus, and Clostridium, all of which can play a substantial role in promoting obesity **[25]**. Specifically, these obesogenic microbes can contribute to weight gain by producing short-chain fatty acids (SCFAs) like butyrate, which provide additional energy to the host. Increased abundance of certain *Firmicutes*, particularly *Faecalibacteriumprausnitzii*, and *Ruminococcus*, is often observed in individuals with obesity. These microbes can enhance energy extraction from the diet. Additionally, metabolites produced by intestinal microbiota can induce low-grade inflammation, further complicating the obesity landscape **[25]** Furthermore, genetic factors and epigenetic variations significantly

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influence the relationship between gut microbiota composition and its role in obesity and metabolite production.

2. Diabetes Mellitus

Diabetes mellitus significantly impacts global health, with risk factors including family history, poor diet, and obesity. The rise in urbanization, dietary changes, and unhealthy lifestyles contribute to the increasing incidence of diabetes, making it a global crisis. About 422 million people worldwide have diabetes, the majority living in low-and middle-income countries, and 1.5 million deaths are directly attributed to diabetes each year. Recent research indicates that diabetes progression is closely linked to changes in the intestinal microbiota composition **[26]**. Diet plays a crucial role in shaping the intestinal microbiota and is a significant factor in diabetes development **[27]**. Certain species of Bacteroides, such as *Bacteroidesfragilis*, may be associated with improved insulin sensitivity, while dysbiotic forms can contribute to insulin resistance and higher levels of *Prevotella* have been linked to metabolic dysregulation and inflammation, often seen in type 2 diabetes.

The influence of microbiota on type 2 diabetes is mediated through mechanisms involving changes in butyrate and in cretin secretions **[28]** In type 2 diabetes patients, studies have shown moderate intestinal microbial dysbiosis, a decrease in butyrate-producing bacteria, and an increase in opportunistic pathogens **[28]**. Other research highlights the significant impact of gut microbiota on type 2 diabetes pathways, including insulin signaling, inflammation, and glucose homeostasis **[29]**. However, further studies are needed to fully understand the mechanisms and the influential role of gut microbiota in diabetes development.

3. Cardiovascular Disease-Related Microbiota

Heart disease remains a leading cause of death worldwide, with its prevalence expected to rise, particularly in low and middle-income countries. The pathophysiology and progression of cardiovascular diseases (CVDs) also involve the intestines, mainly due to reduced blood flow leading to intestinal barrier dysfunction. The intestinal endothelial barrier is regulated by various mechanisms, including a well-balanced intestinal microbiota **[30]**. Recent studies have highlighted the role of intestinal microbiota in heart disease and stroke **[31, 32]**. Emerging evidence indicates that gut dysbiosis is linked to the production of numerous metabolites by intestinal microbiota, which disrupts the function of the gut endothelial barrier. Increased populations of *Escherichia coli* and other *Enterobacteriaceae* are often linked to inflammation and cardiovascular risk factors **[33]**. *Faecalibacterium* Reduced levels of *Faecalibacteriumprausnitzii* are associated with increased cardiovascular risk, possibly due to its anti-inflammatory properties**[34]**.

4. Inflammatory Bowel Disease (IBD)

Inflammatory bowel disease is prevalent in Western countries and is rapidly increasing in newly industrialized regions like Asia, the Middle East, Africa, and South America **[35]**. Recent advancements have highlighted the role of gut microbiota in the pathogenesis of IBD. Studies show that patients with IBD often have decreased diversity in their intestinal microbiota, particularly a reduction in *Firmicutes*and *Proteobacteria***[36]**. This imbalance is linked to abnormal immune responses and various intestinal disorders. Consequently, modifying gut microbiota to restore immunological balance is being explored as a potential treatment strategy for IBD **[37]**. Alterations in the abundance of *Clostridium* species, particularly *Clostridium difficile*, can exacerbate IBD symptoms and are often found in dysbiotic states.

5. Hypertension-Related Microbiota

Hypertension is a threat to public health **[38]**. ‘Studies have shown that various genetic and environmental factors, including dietary salt intake, lack of exercise, and alcohol consumption, also contribute to hypertension progression **[39]**. Moreover, alterations in the composition of the intestinal microbiota can result in the development of novel antihypertensive therapies.’ ‘The various mechanisms underlying the relationship between gut microbiota and hypertension have been proposed, although there is no definite understanding.’ The ratio of *Bacteroidetes* and *Firmicutes* within intestinal microbiota has been significantly associated with hypertension **[40]**. *Fusobacterium* have been linked to hypertension and associated inflammatory processes**[41]**. *Lactobacillus* and *Bifidobacterium* Decreased populations of these beneficial bacteria may contribute to hypertension by influencing metabolic health and inflammation **[42]**.

6. Cancer-Related Microbiota

Cancer ranks as the second leading cause of death worldwide **[43]**. Various factors, including exposure to pathogens, UV radiation, toxic substances, diet, and lifestyle, significantly influence cancer risk. The risk is primarily determined by the dosage, duration, and combination of these factors, along with the patient’s genetic background **[44]**. There is increasing interest in understanding the characterization and functionality of intestinal microbiota due to its complex relationship with the host **[45]**. Research has shown that disruption or alteration of gut microbiota plays a significant role in the development of colorectal cancer in both genetic and carcinogenic tumor genesis models **[44]**. Studies in metabolomics and metagenomics have highlighted the dual role of gut microbiota in reducing cancer risk and promoting tumor growth, as well as its impact on anti-cancer therapies **[46]**. Alterations in the abundance of these genera are observed in colorectal cancer, potentially influencing tumor development through inflammation and metabolism. *Fusobacteriumnucleatum* is specifically linked to colorectal cancer, elevated levels of this bacterium may promote tumorigenesis**[47]**.

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