Community Acquired Infection

REVIEW ARTICLE

Navigating dysbiosis: Insights into gut microbiota disruption and health outcomes

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ABSTRACT

Dysbiosis is a condition of microbial imbalance marked by an overabundance of pathogenic microbes and decreased microbial diversity, which influences the composition and function of the gut microbiome and can seriously impair physiological functions. Dietary interventions are important, especially those high in fiber and prebiotics, which increase microbial diversity and encourage the growth of good bacteria. The effectiveness of fecal microbiota transplantation (FMT) in treating recurrent *Clostridium difficile* infections has drawn attention, and it is being investigated for additional dysbiosis-related illnesses. There are still issues, though, such as the absence of accepted diagnostic standards for dysbiosis, the variation in how each person reacts to treatments, and doubts about certain treatments' long-term effects and safety. The development of reliable, standardized diagnostic instruments should be prioritized in future research to precisely diagnose dysbiosis and evaluate treatment results. Furthermore, customized medication strategies should be prepared, utilizing developments in microbiome analysis to customize interventions according to each patient's unique microbiome composition and medical state. In this context, translating scientific discoveries into useful applications that improve gut health will require interdisciplinary partnerships between microbiologists, physicians, dietitians, and public health specialists. To further the field, this review explores the impacts of gut microbiota dysbiosis on human health and discusses potential therapeutic interventions.

Key words: dysbiosis, microbiota, fecal microbiota transplantation

INTRODUCTION

The term "human microbiota" describes the diverse population of microorganisms that live in different areas of the human body, especially the gut, including bacteria, viruses, fungi, and archaea.[1,2] The human microbiota plays a vital role in health by assisting with metabolic processes including digestion, homeostasis maintenance, vitamin synthesis, immune system regulation and immunological responses, and pathogen defense through competitive exclusion. This underscores its potential for both illness prevention and therapy.[3,4]

Autoimmune disease development may be influenced by the microbiome, and inflammatory bowel diseases (IBDs) have been connected through the gut–brain axis to dysbiosis in the microbiota composition, as have metabolic disorders, including obesity and type 2

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Received: 12 November 2024; Revised: 3 March 2025; Accepted: 18 March 2025
https://doi.org/10.54844/cai.2024.0778

diabetes, and mental health issues. Dysbiosis is the term used to describe an imbalance in the makeup and activity of the microbial communities in the body, especially in the gut, which results in an overabundance of dangerous microbes and a decline in good ones. There can be numerous causes of this disruption in balance, such as poor food, stress, antibiotic usage, and environmental changes. The potential for dysbiosis to impair immunological responses, metabolic processes, and the general equilibrium highlights the crucial need to maintain a healthy microbiota for optimal health results. In the event of disease, as dysbiosis plays a major part in its pathophysiology, microbiota-targeted treatments may improve health and restore equilibrium.[5]

Against that background, this narrative review comprehensively overviews the current understanding of dysbiosis, providing its description, underlying causes, and various effects on human health. In particular, the contributions of environmental variables, antibiotics, diet, and lifestyle to microbial imbalance are investigated. The review emphasizes the negative effects of dysbiosis and its connections to numerous illnesses, including autoimmune diseases, mental health difficulties, and metabolic abnormalities. It also assesses prospective therapeutic approaches, including dietary changes, fecal microbiota transplantation (FMT), probiotics, and prebiotics, for reestablishing microbiome balance. By compiling the latest data, this review offers improved knowledge of dysbiosis and guides future studies and therapeutic procedures using microbiota management to improve health outcomes.

COMPOSITION OF HUMAN MICROBIOTA

The composition of the microbiota differs greatly throughout the sites in the body, reflecting the distinct habitats and roles of each site. (1) Gut microbiota: the most varied and densely populated microbiota is found in the gut, where bacteria mainly belonging to the phyla *Firmicutes*, *Bacteroidetes*, *actinobacteria*, and *proteobacteria* are found. This community is essential for immunological control, metabolism, and digestion. The composition varies greatly from person to person and is affected by age, health, and diet. (2) Skin microbiota: affected by variables such as temperature, moisture, and sebaceous gland activity, the skin microbiota is varied and differs across body parts. *Propionibacterium*, *corynebacterium*, and *Staphylococcus* are common bacterial genera. the skin is a barrier, and its microbiota influences immune responses and provides protection from infections.[6] (3) Oral microbiota: a diverse microbial community comprising bacteria, fungi, and viruses is found in the mouth cavity.[7] *Fusobacterium*, *Neisseria*, and *Streptococcus* are important genera. standing as a major factor in oral health and disorders including dental caries and periodontitis, its composition differs between the various sites of the mouth (teeth, tongue, and gums) and can be influenced by nutrition, oral hygiene, and systemic health. (4) Respiratory microbiota: Although it is less varied than the oral or gut microbiota, the respiratory tract microbiome is nonetheless crucial to respiratory health. It includes genera such as *Moraxella*, *Haemophilus*, and *Streptococcus*. Asthma and chronic obstructive lung disease have been associated with dysbiosis in this region, and environmental variables, smoking, and infections can affect the composition.[8] (5) Urogenital microbiota: Urogenital microbiota varies between men and women and is impacted by sexual activity, hormone fluctuations, and personal cleanliness habits. *Lactobacillus* species are common in the vaginas of females and help prevent infections by keeping the environment acidic. The microbial diversity of the urinary system is generally lower in males. Urinary tract infections and other problems related to reproductive health can be exacerbated by dysbiosis in this region.[9]

FUNCTIONS OF MICROBIOTA IN HEALTH

Digestive health

Complex carbohydrates and fibers indigestible by human enzymes are fermented with the help of microbiota. They generate short-chain fatty acids (SCFAs), including butyrate, propionate, and acetate, which give colon cells energy and support a healthy intestinal lining.[10] In addition to their anti-inflammatory qualities, SCFAs also regulate gut motility and general gut health (Figure 1).

Immune system regulation

The development and regulation of the immune system depend heavily on the gut microbiota. It promotes a balanced immune response and inhibits hyperactive reactions, which can result in allergies or autoimmune illnesses, by aiding in the development of immune cells and the synthesis of immunoglobulin A (IgA).[11]

Defense against infections

In the gut, beneficial microorganisms vie with pathogens for resources and attachment sites. As a first defense against infections, they can also create bacteriocins and other antimicrobial compounds that inhibit harmful bacteria.[12]

Metabolism and absorption of nutrients

The microbiota facilitates the production of vitamins necessary for metabolic activities as well as the absorption of nutrients.[13] For example, some gut bacteria produce B vitamins, essential for energy metabolism, and vitamin K, for blood coagulation.

Impact on mood and mental health

According to the gut–brain axis, there is a two-way communication channel between the brain and the gut

Figure 1. Functions of microbiota.

bacteria. Neurotransmitters such as serotonin and gamma-aminobutyric acid (GABA), which regulate mood and cognitive function and may impact disorders such as anxiety and depression, can be produced by gut flora.[14]

Detoxification

By metabolizing and detoxifying xenobiotics, such as medications and environmental pollutants, certain gut bacteria can lessen the likelihood of those negatively impacting the body. Several drugs' bioavailability and effectiveness may be altered by this mechanism.[15]

MECHANISM AND CAUSES OF DYSBIOSIS

Pathologic infections and dysbiosis

By disrupting the balance of the microbiota, pathologic infections caused by bacteria, viruses, and fungi can result in dysbiosis (Table 1). These diseases show the complex interactions between microbial communities and infections, the former of which are brought on by altering the composition of microorganisms, promoting the development of pathogenic organisms, and inducing systemic inflammation.

Disruption of microbiota by antibiotics and other medication

The balance of the microbiota can be significantly disrupted by antibiotics and several other medications, leading to dysbiosis (Table 2).

Diet and lifestyle factors

By altering the diversity and makeup of the microbiota, dietary practices, chronic stress, excessive alcohol consumption, and other lifestyle factors all contribute significantly to dysbiosis. To preserve a healthy gut microbiome and prevent associated health issues, these factors need to be taken care of (Table 3).

Host genetics and immune system interactions contributing to dysbiosis

Interactions between the immune system and host genetics have a major impact on the composition and function of the microbiota (Table 4). Immunological responses involving innate or adaptive immunity can either promote or inhibit dysbiosis, and genetic predispositions influence microbial diversity. Knowing these interactions is essential to creating strategies to maintain a healthy microbiome and reduce health issues linked to dysbiosis.

IMPACTS OF DYSBIOSIS ON HUMAN HEALTH

Dysbiosis and gastrointestinal disorders: the role in irritable bowel syndrome (IBS), IBD, and colorectal cancer

An imbalance in the gut microbiota, known as dysbiosis, is typified by alterations in the makeup of bacterial communities and a decline in microbial diversity. This has frequently been linked to numerous gastrointestinal conditions, such as colorectal cancer, IBD, and IBS. Gaining knowledge of how dysbiosis exacerbates such disorders may help develop possible treatment approaches (Figure 2).

Dysbiosis and IBS

The symptoms of IBS, a functional gastrointestinal illness, include bloating, changed bowel patterns, and abdominal pain. Dysbiosis is a key factor in the pathophysiology, with people with IBS frequently having higher concentrations of potentially harmful bacteria such as *Escherichia coli* and

Table 1: Various pathological infections responsible for dysbiosis

Type of infection	Pathogen	Mechanism of dysbiosis	Reference
Bacterial	*Clostridium difficile*	Due to the disruption of normal gut flora caused by antibiotic use, *C. difficile* can multiply and create inflammatory toxins	[16]
	EHEC	Produces the Shiga toxin, which outcompetes good bacteria and causes intestinal inflammation and dysbiosis	[17]
	Helicobacter pylori	Changes the composition of the gastric microbiota by causing persistent inflammation in the stomach	[18]
Viral	HIV	Modifies the gut microbiome, increasing the risk of opportunistic infections by causing systemic inflammation and microbial translocation	[19]
	Influenza virus	Alters the respiratory microbiome, which increases vulnerability to secondary infections and encourages the growth of harmful microorganisms	[20]
Fungal	*Candida albicans*	Dysbiosis causes overgrowth in immunocompromised people, which can result in illnesses including candidiasis and oral thrush	[21]
	Aspergillus species	Alters the lung flora and contributes to further difficulties by causing respiratory infections in immunocompromised patients	[22]

ECHC, *Escherichia coli*; HIV, Human Immunodeficiency Virus.

Table 2: Antibiotics and other medications that disrupt microbiota

Medication type	Mechanism of disruption	Impact on microbiota	Reference
Antibiotics	Kill or inhibit a wide range of bacteria, often indiscriminately	- Reduce microbial diversity. - Allow overgrowth of opportunistic pathogens (*e.g.*, *Clostridium difficile*)- Alter nutrient metabolism and SCFA production	[23]
PPIs	Reduce stomach acid production, increasing gastric pH	- Create a more hospitable environment for pathogenic bacteria- Increase risk of gastrointestinal infections	[24]
NSAIDs	Cause gut mucosal damage and alter gut permeability	- May lead to dysbiosis and exacerbate conditions such as IBD	[25]
Antidepressants	Influence gut motility and secretion of gut hormones	- Can lead to changes in microbiota, potentially impacting mood disorders	[26]
Immunosuppressants	Suppress the immune system, altering microbial control	- May increase susceptibility to infections and change microbiota composition	[25]

IBD, inflammatory bowel disease; NSAIDs, non-steroidal anti-inflammatory drugs; PPIs, proton pump inhibitors.

Table 3: Effect of diet and lifestyle factors on dysbiosis

Factor	Description	Impact on dysbiosis	Reference
Dietary patterns	High-Fat diets	Cause inflammation by decreasing microbial diversity and encouraging the growth of dangerous germs	[26]
	High-Sugar diets	Cause harmful bacteria and yeast to proliferate, preventing the establishment of good species	[27]
	Low-Fiber diets	Impact the function of the intestinal barrier, lower microbial diversity, and restrict the generation of SCFA	[28]
	Processed foods	Cause irritation and change the makeup of microorganisms through their preservatives and chemicals	[29]
Stress	Chronic stress	Increases intestinal permeability and modifies gut motility, which permits infections to move	[30]
	Hormonal changes	Impacts immunological response and gut microbiota composition	[31]
Alcohol consumption	Excessive alcohol intake	Increases intestinal permeability, changes the gut microbiota, and encourages the proliferation of dangerous microorganisms	[32]
	Impact on liver and gut health	Exacerbates dysbiosis by harming the liver and intestinal lining	[33]
Lifestyle factors	Sedentary lifestyle	Decreases gut health and lowers microbial diversity, which can lead to metabolic disorders and dysbiosis	[34]
	Sleep disturbances	Adversely impact gut microbiota, resulting in imbalances that affect health and mood	[35]
	Smoking	Associated with decreased microbial diversity and harmful bacterial dominance	[36]

SCFA, short-chain fatty acid.

Table 4: Host genetic factors' and immune system interactions' dysbiosis contributions

Factor	Description	Impact on dysbiosis	References
Genetic factors	Heritability of microbiota	Genetic predisposition influences the diversity and composition of the microbiota, leading to variations in gut health	[37]
	Metabolic and immune genes	Variations in genes related to metabolism and immune function can affect microbial composition and dysbiosis susceptibility	[38]
Immune system interactions	Innate immunity	Overactive innate immune responses can cause chronic inflammation, promoting dysbiosis	[39]
	Adaptive immunity	Imbalances in T-helper-cell responses can alter microbiota composition and contribute to conditions such as allergies	[40]
Microbiota-immune interactions	Microbiota-driven immune responses	The microbiota can modulate immune responses, stimulating regulatory T-cell production and helping maintain immune tolerance	[41]

lower abundances of helpful bacteria such as *Lactobacillus* and *Bifidobacterium*.[42] Through the synthesis of metabolites and neurotransmitters, dysbiosis may interfere with the gut–brain axis, affecting gut motility and sensitivity. IBS symptoms may worsen due to this interaction,[43] and they may be exacerbated by dysbiotic bacteria which cause low-grade inflammation.[44]

Dysbiosis and IBD

IBD includes diseases that cause persistent inflammation of the gastrointestinal system, such as Crohn's disease and ulcerative colitis. Microbial diversity is frequently significantly reduced in IBD patients. Taxa with anti-inflammatory characteristics, including *Faecalibacterium prausnitzii*, are frequently reduced.[45] Pathogenic organisms can flourish and cause inflammation when beneficial microbes that typically maintain gut homeostasis are reduced due to dysbiosis, resulting in an inappropriate immune response.[46] The production of SCFAs, such as butyrate, which are essential for preserving the intestinal barrier's integrity and regulating immunological responses, might be impacted by changes in gut microbiota.[47]

Dysbiosis and colorectal cancer

Recent data point to a connection between colorectal cancer development and dysbiosis. Certain toxins and secondary bile acids, which can harm the intestinal epithelium and encourage carcinogenesis, provide examples of carcinogenic metabolites that the dysbiotic microbiota may create.[48] Dysbiosis-induced chronic inflammation can alter the gut's biological environment and encourage the growth of cancer.[49] The local immunological environment may also be impacted by dysbiosis, making it more difficult to identify and react to cancerous cells.[50]

Dysbiosis and metabolic diseases: the connections to obesity, diabetes, and metabolic syndrome

Type 2 diabetes, obesity, and metabolic syndrome, among other metabolic illnesses, are significantly influenced by dysbiosis in the gut microbiota, specifically its impact on microbiota control of energy homeostasis, metabolism, and systemic inflammation.

Dysbiosis and obesity

People who are obese frequently have a unique microbiota profile defined by a large ratio of *Firmicutes* to *Bacteroidetes*. Increased energy collection from dietary components is linked to this change. Bile acids and SCFAs, which are essential for energy metabolism, can be produced by dysbiotic microbiota. Obesity may result from decreased SCFA-producing bacteria, which compromises the integrity of the intestinal barrier and raises inflammation.[51] Here, an imbalance in the gut microbiota can lead to weight gain and metabolic dysregulation by boosting systemic inflammation, which results from increasing intestinal permeability and enabling endotoxins to enter the bloodstream and initiate inflammatory pathways.[52]

Dysbiosis and type 2 diabetes

Studies link dysbiosis to an altered microbial composition and reduced microbial diversity in those with type 2 diabetes. Insulin resistance has been associated with specific bacterial taxa, including *Prevotella*.[53] The gut microbiota affects glucose metabolism and may improve insulin sensitivity by influencing the synthesis of SCFAs and other metabolites. In this context, dysbiosis may cause a chronic low-grade inflammatory state resulting when gut permeability increases circulating lipopolysaccharide (LPS) levels[54] exacerbating insulin resistance and contributing to the pathophysiology of type 2 diabetes, and it may decrease the generation of SCFAs, affecting glucose homeostasis.[55]

Dysbiosis and metabolic syndrome

Obesity, insulin resistance, dyslipidemia, and hypertension are among the disorders that make up metabolic syndrome and whose emergence is partially the result of dysbiosis. For instance, dyslipidemia can result from changes in the gut microbiota impacting lipid metabolism; in particular, lipid profiles may be impacted by microbial populations that affect the production of

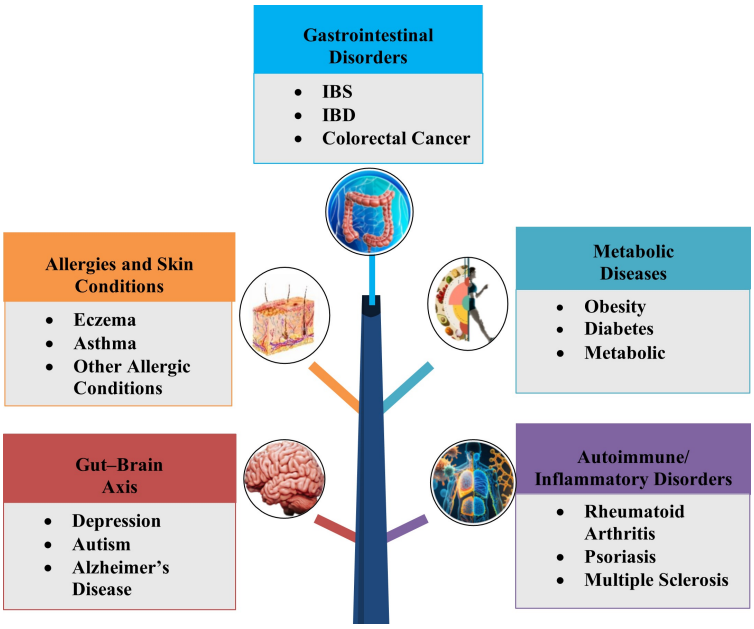

Figure 2. Impacts of dysbiosis on human health. IBD, inflammatory bowel disease; IBS, irritable bowel syndrome.

lipoproteins and the absorption of dietary fats.[56] Additionally, dysbiosis plays a role in endotoxemia and systemic inflammation, which contribute to obesity and diabetes in metabolic syndrome. Moreover, cardiovascular problems linked to metabolic syndrome can arise from metabolic pathways' disruption in the chronic inflammatory state caused by dysbiosis.[57]

Dysbiosis and autoimmune/inflammatory disorders: connections to rheumatoid arthritis (RA), psoriasis, and multiple sclerosis (MS)

Increasingly, autoimmune and inflammatory diseases have been connected to dysbiosis in the gut microbiota. Changes in the microbial diversity and composition, affecting inflammation and immunological responses, define this relationship. Herein, we examine the connections between dysbiosis and three distinct illnesses: MS, psoriasis, and RA.

Dysbiosis and RA

RA is a chronic inflammatory disease that mostly affects the joints. The gut microbiota composition of RA patients is often different from that of healthy controls, with more pathogenic and fewer varied bacteria.[58] Interestingly, a higher abundance of *Prevotella copri* has been associated with the onset of RA. In this context, dysbiosis may affect systemic inflammation by changing immune responses. Certain gut bacteria can affect T-cell development, creating a pro-inflammatory milieu and contributing to RA pathogenesis.[59] Moreover, "a leaky gut" describes the elevated intestinal permeability observed in individuals with RA. In that way, this disease may cause microbial antigens to enter the circulation, triggering an autoimmune reaction.[60]

Dysbiosis and psoriasis

Chronic inflammatory skin disorder known as psoriasis is characterized by red, scaly areas. The gut microbiome of psoriasis patients frequently exhibits less microbial diversity. Bacterial taxa linked with anti-inflammatory qualities are decreased,[61] and dysbiosis may exacerbate the persistent inflammation in psoriasis. Dysbiotic microbiota may also affect T-cell activation and cytokine production, exacerbating systemic inflammation, for instance, through the altered expression of pro-inflammatory cytokines such as TNF-α, which are essential in psoriasis.[62] This underpins the theory of the gut–skin axis, whereby dysbiosis contributes to skin disorders by causing systemic inflammation. Moreover, microbial metabolites may impact immune responses and epidermal barrier integrity, exacerbating psoriasis.[63]

Dysbiosis and MS

One autoimmune condition affecting the central nervous system is MS, and the gut microbiome of MS patients differs significantly from that of healthy people, with pro-inflammatory taxa increasing and beneficial bacteria such as *Faecalibacterium prausnitzii* decreasing.[64] Dysbiosis may impact the onset and course of MS through its effects on immune cell activation and differentiation, influencing the balance between pro-inflammatory and regulatory T cells, which can alter the autoimmune response and produce the specific response characterizing MS.[65] Moreover, dysbiosis-induced increases in circulating bacterial products, such as LPSs, can cause neuroinflammation and aid in the demyelination process seen in MS.

The gut-brain axis and its influence on neurological and psychiatric disorders

The central nervous system and the gastrointestinal tract are connected by a bidirectional communication network known as the gut-brain axis, which combines immunological, hormonal, and neuronal signals and is coming to be widely acknowledged for its involvement in numerous neurological and mental illnesses. For instance, information about the condition of the gut, such as the presence of nutrients and microbial metabolites, is transmitted to the brain mostly through the vagus nerve. Meanwhile, the gut microbiota affects the immune system by regulating systemic inflammation and the synthesis of neuroactive compounds. Moreover, gut-derived chemicals, such as ghrelin and serotonin, can influence mood control and brain function. When the gut–brain axis is upset by dysbiosis, this may trigger disorders such as depression, autism spectrum disorder (ASD), and allergic reactions.

Dysbiosis and depression

People with depression often have altered gut microbiota profiles, marked by low diversity and a decline in bacterial taxa linked to mood regulation.[66] For example, depression symptoms have been associated with decreased levels of *Lactobacillus* and *Bifidobacterium*. Furthermore, neurotransmitters essential for mood control, such as serotonin, can be produced by gut microbes, and dysbiosis can interfere with their manufacturing by the gut (*e.g.*, 90% loss in serotonin production), leading to depression symptoms.[67] At the same time, increased intestinal permeability brought on by dysbiosis may allow endotoxins, such as LPSs, to enter the bloodstream and fuel systemic inflammation, which has been linked to the etiology of depression.[68]

Dysbiosis and ASD

The gut microbiome of children with ASD differs significantly from that of neurotypical children. Among the variations include decreased microbial diversity and changed bacterial abundances.[69] Here, dysbiosis may impact the synthesis of metabolites critical for brain growth and health, such as SCFAs, affecting neuroinflammatory behavior and processes. Meanwhile, microbial antigens may translocate *via* increased gut permeability in ASD patients, eliciting immunological reactions that impact behavior and brain functioning.[70]

Dysbiosis and Alzheimer's disease (AD)

AD, a progressive neurodegenerative illness characterized by memory loss and cognitive decline, has been linked to dysbiosis in the gut microbiota. Compared to healthy controls, people with AD frequently exhibit significantly altered gut microbiota, including decreased microbial diversity and changes in certain bacterial taxa, such as a rise in *Fusobacterium* and a fall in *Bifidobacterium*.[71] Increased intestinal permeability brought on by dysbiosis can allow toxins and microbial metabolites into the bloodstream, causing systemic inflammation and contributing to the neuroinflammatory processes characterizing AD.[72] Furthermore, modifications in microbiota may affect the onset and course of AD *via* pathways such as amyloid pathology, inflammation, and the gut-brain axis. In the latter case, dysbiosis can impact mood, cognition, and behavior by disrupting this axis, which allows neuroactive chemicals produced by gut bacteria to be transmitted *via* many communication channels, such as the vagus nerve.[73]

The role of microbiota imbalance in allergies and skin conditions

Eczema and asthma are among the many allergic disorders significantly influenced by microbiota dysbiosis, which impacts the immune system, inflammation, and the general well-being of the skin and respiratory system. We provide a summary of the links between dysbiosis and these disorders below.

Dysbiosis and eczema (atopic dermatitis)

People with eczema frequently have lower microbial diversity in their guts and on their skin than people without the condition. In particular, eczema severity has been associated with decreased helpful bacteria, including *Bifidobacterium* and *Lactobacillus*.[74] In these ways, increased transepidermal water loss and an increased vulnerability to allergens can result from dysbiosis's impairment of the skin barrier. Moreover, eczema symptoms and inflammation can be worsened by an imbalance that encourages the colonization of harmful bacteria such as *Staphylococcus aureus*.[75] Changes in the gut microbiota may also impact systemic immune responses *via* the gut–skin axis, which dysbiosis may skew toward a Th2-dominant profile, linked to allergic diseases such as eczema.[76]

Dysbiosis and asthma

The asthma risk is influenced by the composition of the gut microbiota throughout early life. Asthma development has been connected to dysbiosis, defined by decreased variety and elevated potentially harmful bacteria, whereas a diverse microbiome during infancy is linked to a lower risk of asthma.[77] Here, airway inflammation and hyperreactivity can be exacerbated by dysbiosis, which can cause an imbalance in immunological responses. Specifically, asthma symptoms may be exacerbated by systemic immune responses resulting from allergens entering the bloodstream through increased intestinal permeability brought on by dysbiosis.[78] Asthma inflammation may worsen if dysbiosis reduces SCFA synthesis, since the production of SCFAs by a healthy gut microbiota has anti-inflam-

matory properties and is a crucial support for immunological homeostasis.[79]

Dysbiosis and other allergic conditions

As an imbalance in nasal microbiota might affect local immune responses, dysbiosis is also linked to allergic rhinitis. Increased vulnerability to allergic rhinitis has been linked to a decreased diversity of microorganisms in the nasal cavity.[80] It has been demonstrated in the literature that food allergies may emerge from early-life dysbiosis, just like other allergic diseases; here, a varied gut microbiota during infancy fosters tolerance to dietary antigens, whereas dysbiosis may result in sensitization and allergic reactions.[81]

CURRENT AND EMERGING DIAGNOSTIC TECHNIQUES

Microbiome profiling and sequencing in studying dysbiosis

Microbiome analysis is required to understand the intricate communities of microorganisms in diverse habitats, and this applies to the study of dysbiosis and its impact on health. Accordingly, microbiome investigations frequently cutting-edge methods such as metagenomics, metabolomics, and 16S rRNA sequencing. Here is a summary of those methods and their applications.

16S rRNA Sequencing

Particularly in studies on dysbiosis, 16S rRNA sequencing is a widely used method for describing bacterial communities in various contexts. This method focuses on the highly conserved 16S ribosomal RNA gene, which contains variable regions that enable taxonomic differentiation among bacterial species.

The variety and composition of microorganisms can be characterized by amplifying and sequencing the variable sections, which allows researchers to identify and quantify the different bacterial species present in a sample. By using 16S rRNA sequencing, one can detect shifts in the relative abundances of specific bacteria in dysbiosis, which could indicate imbalances connected to illnesses like obesity or IBD.[82] This method provides information on the diversity of bacteria, but it is not always able to detect species-level differences or non-bacterial microorganisms like *viruses* and *fungi* due to resolution problems.

Metagenomics

Metagenomics, which directly sequences each DNA molecule in a sample, provides a more comprehensive approach to microbiome research. This enables researchers to acquire a thorough understanding of the entire microbial community, which comprises *bacteria*, *fungi*, *viruses*, and *archaea*. For example, metagenomics can identify genes associated with virulence factors, antibiotic resistance, and metabolic pathways, enabling scientists to investigate the microbiome's functional potential. One of the technique's primary applications, it is particularly useful for understanding how host metabolism and immune responses are affected by dysbiosis. However, because of the intricacy of the data produced, metagenomics requires the use of advanced bioinformatics tools for analysis, making it resource-intensive and challenging to understand.[83]

Metabolomics

Metabolomics is the study of metabolites in biological samples, revealing the metabolic outputs of the microbiome and their impact on host physiology. Thus, by examining the metabolites generated by gut microbes, scientists might discover how dysbiosis affects metabolic pathways and potentially link certain metabolites to illnesses like diabetes and neurological diseases. Additionally, this method can assist in identifying metabolites that function as biomarkers for numerous dysbiosis-related disorders.[84–89] However, despite its promise, metabolomics has the drawback that metabolite levels can differ greatly depending on factors such as heredity, nutrition and environmental impacts, making it difficult to understand and analyze the collected data.

Biomarkers of dysbiosis

Table 5 described biomarkers used for diagnosing of dysbiosis and assessing treatment efficacy.

Therapeutic approaches to restoring microbial balance

Probiotics

Probiotics are live bacteria that provide health benefits to the host when given in sufficient quantities. They are mostly present in dietary supplements and fermented foods such as kefir, sauerkraut, and yogurt. Probiotics can aid in reestablishing the normal balance of the gut microbiota when it has been upset by factors such as stress, poor diet, and antibiotic use. Certain strains, including *Lactobacillus* and *Bifidobacterium*, lessen dysbiosis-related gastrointestinal symptoms such as gas, bloating, and irregular bowel movements and enhance gut health.[102] Certain probiotic strains improve the gut barrier function and have anti-inflammatory benefits. Moreover, probiotics dramatically reduce the symptoms of IBS, a disorder frequently associated with dysbiosis, according to a meta-analysis.[103]

Probiotics help many people, but not everyone has the same benefits. The strain used, its dosage, and the person's gut microbiota are among the variables affecting the degree to which probiotics are beneficial. This implies that probiotic therapy targeted to the makeup of each person's microbiome offers an individu-

Table 5: Emerging biomarkers used for diagnosing dysbiosis and assessing treatment efficacy

Biomarker	Description	Role in diagnosis	Role in treatment assessment	Reference
SCFAs	Products of fermentation by gut bacteria	Indicate microbial activity and health	Assess effectiveness of dietary interventions	[90,91]
Fecal calprotectin	Marker of intestinal inflammation	Indicates gut inflammation often associated with dysbiosis	Monitors inflammation levels during treatment	[92,93]
Bacterial DNA markers	Specific DNA sequences from key bacterial species	Detect overgrowth or absence of specific microbes	Track shifts in specific bacterial populations	[94,95]
Immune markers (*e.g.*, cytokines)	Proteins involved in immune response	Indicate immune dysregulation linked to dysbiosis	Evaluate changes in immune response post-treatment	[96,97]
Microbial endotoxins	Components of bacterial cell walls (*e.g.*, LPS)	Indicate translocation of bacteria across gut barrier	Assess gut permeability changes with treatment	[98,99]
Dysbiosis index	Composite score based on various microbial factors	Quantifies dysbiosis severity	Measures shifts in dysbiosis severity post-treatment	[100,101]

LPS, lipopolysaccharide; SCFAs, short-chain fatty acids.

alized method of treating dysbiosis. To date, however, some patients see little to no improvement, which emphasizes the need for further study to determine which strains work best for particular dysbiotic situations. Furthermore, questions have been raised concerning the safety of probiotics in immunocompromised people, highlighting the significance of seeking medical advice before beginning a probiotic supplementation regimen.[104]

Prebiotics

Prebiotics are indigestible food ingredients, mostly dietary fibers, that support the development and function of good gut flora. Prebiotics are frequently found in whole grains, garlic, onions, and bananas. Prebiotics increase microbial diversity and promote the growth of advantageous strains such as *Lactobacilli* and *Bifidobacteria* by acting as probiotic fuel. Prebiotics can improve gut health, in general and dysbiosis, in particular by modifying the composition of the gut microbiota.[105] SCFAs, which are essential for gut health, are produced when gut bacteria ferment prebiotics. These SCFAs can improve nutrient absorption, lower inflammation, and fortify the intestinal barrier. Prebiotic-rich meals have been linked to increased SCFA-producing bacteria, which improves the gut health and lessens dysbiosis symptoms. Hence, eating a diet high in prebiotics significantly altered the makeup of gut microbiota and improved metabolic indicators in overweight people.[106] Despite their advantages, though, not all prebiotics work in the same way, and individual reactions can depend on the makeup of the gut microbiota and general health. When taking large doses of prebiotics, some people may feel gastrointestinal discomfort, including bloating, especially if they have IBS. To maximize prebiotics' benefits for treating dysbiosis, they should be administered gradually and tracking performed of each person's tolerance.[107]

Synbiotics

Synbiotics are a blend of pre- and probiotics intended to improve gut health in concert, based on the idea that probiotics are more effective if prebiotics supports their growth in the gastrointestinal system. Compared to pro- or prebiotics alone, synbiotics may thus more significantly improve the composition and function of the gut microbiota.[108] This synergistic effect is especially pertinent in controlling dysbiosis, as both beneficial bacteria and their food sources are necessary for good gut health. Positive results from synbiotic therapies have been documented in numerous clinical investigations, especially for disorders such as IBD and IBS, whose symptoms have been reduced compared to using a placebo.[109]

These results imply that by targeting the microbial population and its controlling dietary elements, synbiotics may provide a holistic strategy for reestablishing gut health. However, clinical research findings may be contradictory due to different doses and a lack of standardized formulations. Further research is required to find the best combinations of pro- and prebiotics for different dysbiotic diseases. Furthermore, the effectiveness of synbiotics today may be influenced by individual parameters including age, diet, and health state, underscoring the significance of tailored approaches in dysbiosis treatment.[110]

FMT

Fecal material may be transferred from a healthy donor to a recipient to reestablish a balanced gut microbiome. Strict screening procedures are needed to address safety concerns, especially those related to the spread of infections from donors. This operation is mostly used to treat recurrent recipient *Clostridium difficile* infection, which occurs when antibiotic treatments disturb the gut flora, for which it has success rates of over 80%. Its potential use for other gastrointestinal conditions, including IBS and IBD, is also being investigated; the initial results indicate some advantages, though they are conflicting. FMT has a prospective role in addressing

health disorders connected to dysbiosis, especially as our understanding of the gut microbiome advances. However, further studies are necessary to explore the efficacy and long-term implications of FMT.[111,112]

NEXT-GENERATIONN THERAPEUTICS

The treatment options are changing with new developments in gut health and microbiome management, especially regarding dysbiosis and related disorders. New treatments include microbiota-targeted medications, postbiotics, and engineered probiotics. Postbiotics are bioactive chemicals produced by probiotics during fermentation, which have potential uses in metabolic diseases and IBD, where they provide health advantages such as immune regulation and improved gut barrier function.[113] Meanwhile, genetically altered probiotic strains known as "engineered probiotics" are intended to improve therapeutic efficacy by delivering anti-inflammatory chemicals directly to the gut to treat gastrointestinal disorders.[114] Elsewhere, microbiota-targeted medications comprise substances that interact with the gut microbiota to support health by altering microbial populations or increasing the activity of beneficial bacteria, which offers a strategy for treating inflammatory and metabolic conditions.[115] As our knowledge of the gut microbiota advances, these next-generation therapies are coming to offer more accurate and potent therapeutic alternatives, marking a promising direction in microbiome research.

Dietary interventions

Dietary treatments for managing dysbiosis involve using specific nutritional techniques to support a balanced gut microbiota. For instance, fiber-rich diets, such as those heavy in fruits, vegetables, whole grains, and legumes, can decrease populations of harmful microorganisms while promoting the growth and proliferation of beneficial bacteria. Prebiotics, as non-digestible fibers, nourish these good gut bacteria to improve gut health and microbial diversity. A high-fiber diet may also boost the synthesis of SCFAs, which have anti-inflammatory properties and support gut barrier integrity.[116] Furthermore, a better microbiota and low inflammation can be achieved by consuming fewer processed foods, sugars, and artificial additives. In such ways, dietary changes offer a strategy to help people with dysbiosis regain their microbial balance and enhance their general gut health.

Artificial intelligence (AI) in microbiome research

The human microbiome is closely linked to health and disease, with its dysbiosis having been described as associated with conditions such as IBD. However, the links and associations in this space are complex, and vast quantities of data are available on this topic. Accordingly, AI is increasingly integrated into microbiome research.[117] AI enhances microbiome-related healthcare by identifying microbial changes linked to diseases, improving diagnostics, and aiding personalized treatments.

AI applications in microbiome research

Microbial genome analysis

AI facilitates the identification of new microorganisms, genes, and metabolic pathways and improves the reconstruction of microbial genomes from patient samples.

Predicting and diagnosing diseases

AI-based models aid in the noninvasive classification of conditions like IBD and IBS.

Biomarkers discovery

AI facilitates the identification of biomarkers for patient classification and medication discovery.

Medication discovery

AI models can forecast the postprandial glycemic response, which helps with individualized therapy and dietary regimens in personalized medicine.[118]

AI-powered analytical techniques

Machine learning and deep learning

To forecast diseases, traditional machine learning models like logistic regression and random forest are employed. Pattern recognition in microbiome data is enhanced by deep learning methods like convolutional and graph neural networks.

Omics data integration

For thorough microbiome profiling, AI improves multi-omics integration, encompassing metagenomics, metatranscriptomics, metabolomics, and proteomics.

Network analysis

With the use of neural networks and graph-based models, AI aids in the modeling of microbiome interactions.[119]

CHALLENGES AND FUTURE DIRECTIONS IN DYSBIOSIS

The complexity of the gut microbiome and individual variability are the main causes of difficulty in managing dysbiosis. In this context, it is challenging to correctly diagnose dysbiosis in different groups and circumstances due to the absence of defined diagnostic criteria. Furthermore, our knowledge of how nutrition, lifestyle, genetics, and environmental factors impact gut health is complicated by their interaction. Treatment strategies are

made more difficult by the variation in how each patient reacts to treatments such as FMT, dietary changes, and probiotics. The long-term impact and safety of therapies like FMT and tailored probiotics are also questioned, especially in susceptible groups. Furthermore, because the gut microbiome is dynamic, short-term modifications do not always result in long-term health benefits, which raises concerns about the sustainability of interventions.

Future studies should concentrate on creating reliable, standardized methods for identifying dysbiosis and tracking treatment effectiveness. Advances in sequencing technologies and bioinformatics are essential to map the complexity of the gut microbiome and comprehend its functional roles in health and illness. More effective management of dysbiosis may be possible with personalized treatment techniques, such as food programs and targeted medicines based on individual microbiome profiles. Furthermore, investigating the therapeutic potential of microbiota-targeted medications and postbiotics may offer novel substitutes for conventional probiotics and dietary therapies. Multidisciplinary partnerships between microbiologists, physicians, dietitians, and researchers will be crucial as the field develops to convert research results into applications that enhance gut health and general well-being.

CONCLUSION

In sum, human microbiota dysbiosis is a serious health issue underscoring the complex connection between our gut microbiota and general health. Numerous health problems, including autoimmune illnesses, metabolic diseases, gastrointestinal disorders, and even mental health difficulties, have been linked to this imbalance, which is frequently characterized by increased dangerous bacteria and decreased microbial diversity. It is becoming increasingly clear as research progresses that our gut microbiota is significantly shaped by various factors, including our nutrition, lifestyle, medication use, and environmental exposures. A thorough, individualized strategy that accounts for individual differences in the microbiome composition and function is required to manage dysbiosis effectively. Dietary therapies, especially those high in fiber and prebiotics, hold promise for restoring the microbial balance and encouraging beneficial bacterial growth. Additionally, though they have varying effectiveness, new treatments including probiotics, postbiotics, and microbiome-targeted medications present promising directions for development. FMT also appears promising in certain circumstances, though its safety and long-term consequences are crucial considerations.

The study and treatment of dysbiosis still face obstacles despite these developments. For samples, it is difficult to diagnose dysbiosis in various populations due to the absence of defined diagnostic criteria. Furthermore, more research is needed into the mechanisms underlying individual reactions to therapies. Future studies should focus on creating reliable methods for identifying dysbiosis and investigating the possibilities of personalized medicine, which adjusts treatments according to each patient's unique microbiome composition. Multidisciplinary cooperation between microbiologists, physicians, dietitians, and public health specialists will be essential for converting research results into useful applications. The gut microbiota is an essential part of human health, and we may develop creative solutions that treat dysbiosis holistically to improve gut health and the general quality of life, but these require first advancing our knowledge of dysbiosis and its complex health effects.

DECLARATIONS

Author contributions

Kasar GN: Conceptualization, Writing—Original draft preparation. Rasal PB: Writing—Reviewing and Editing. Mahajan SK, Pagar DS, Surana KR: Conceptualization, Supervision. Sonawane DD, Upaganlawar AB: Supervision, Project administration. All authors have read and approved the final version of the manuscript.

Source of funding

No funding received.

Ethical approval

Not applicable.

Informed consent

Not applicable.

Conflict of interest

Khemchand R. Surana is an Editorial Board Member of the journal. The article was subject to the journal's standard procedures, with peer review handled independently of editor and his research groups.

Use of large language models, AI and machine learning tools

None declared.

Data availability statement

No additional data.

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