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Gut Dysbiosis: A Key Player in Metabolic health Management

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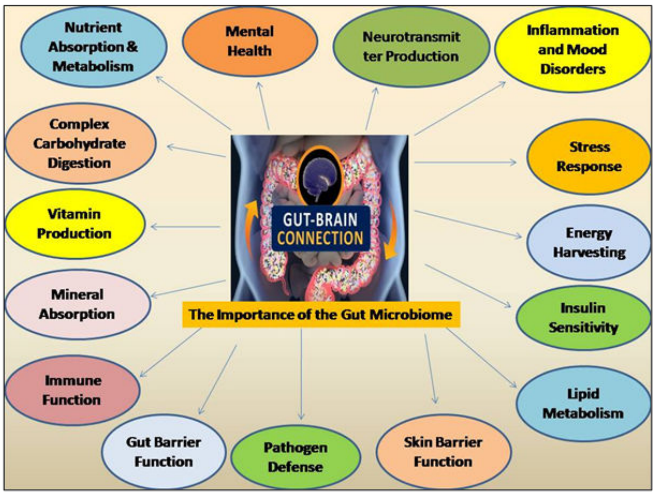
ABSTRACT

Gut dysbiosis, an imbalance in the microbial community of the intestines, has emerged as a significant contributor to metabolic syndrome, a cluster of conditions including obesity, insulin resistance, high blood pressure, and abnormal cholesterol levels. Recent studies indicate that gut dysbiosis can lead to increased inflammation, altered metabolism, and disruptions in the regulation of glucose and lipid levels, thereby promoting the development of metabolic syndrome. Intervention strategies to correct gut dysbiosis and mitigate its impact on metabolic syndrome are gaining attention. Probiotics, prebiotics, dietary changes, and fecal microbiota transplantation (FMT) are among the methods being explored. Probiotics, beneficial bacteria that can be consumed through supplements or fermented foods, help restore a healthy gut microbiome balance. Prebiotics, dietary fibers that feed beneficial gut bacteria, also play a crucial role in maintaining gut health. Additionally, adopting a diet rich in fruits, vegetables, whole grains, and lean proteins can support a healthy microbiome. FMT, a procedure where fecal matter from a healthy donor is transplanted into the gut of a person with dysbiosis, shows promise in restoring microbial balance and improving metabolic outcomes. If it is checked the initial level of Gut dysbiosis and major causes the metabolic syndrome can be prevented. Majority of all life style diseases like diabetes, cardiovascular diseases, Histamine intolerance, thyroid diseases and autoimmune diseases are due to Gut dysbiosis. So, if it is corrected metabolic syndrome may be prevented in the initial stages. These interventions, by targeting gut health, offer potential pathways to alleviate and prevent metabolic syndrome, highlighting the crucial link between gut microbiota and overall metabolic health and personalized medicine.

Keywords: Gut dysbiosis, metabolic syndrome, probiotics, prebiotics, dietary changes, fecal microbiota transplantation (FMT).

GRAPHICAL ABSTRACT



Gut-Brain Connection; A key player in Metabolism and Diseases

INTRODUCTION

It is becoming more well acknowledged that one of the main causes of metabolic syndrome is gut dysbiosis, which is an imbalance in the microbial community of our intestines. A collection of disorders known as metabolic syndrome raise the risk of heart disease, stroke, and type 2 diabetes [1-2]. These disorders include abnormal cholesterol levels, high blood pressure, high blood sugar, and excess body fat around the waist. According to recent studies, gut dysbiosis can have a major effect on our health. Metabolic syndrome can arise from an unhealthy gut microbiome that interferes with the body's capacity to control fat and glucose levels and causes inflammation. This emphasises how important gut flora are for preserving general metabolic health. A number of therapies are being investigated to address gut dysbiosis and its impact on metabolic syndrome. A healthy equilibrium in the gut can be restored with the use of probiotics, which are good bacteria that can be found in fermented foods and supplements. A healthy microbiome is also supported by prebiotics, which are fibres that nourish the beneficial bacteria in our intestines. Changing one's diet to include more fruits, vegetables, healthy grains, and lean proteins can also improve gut health. Faecal microbiota transplantation (FMT), which entails inserting fecal matter from a healthy donor into the gut of a person with dysbiosis, is another potential option. A balanced microbial ecology in the intestines may be restored as a result. We can target the underlying cause of metabolic syndrome and lower its prevalence by concentrating on improving gut health through these therapies, which will improve overall health outcomes [3-5].

GUT DYSBIOSIS, METABOLIC SYNDROME AND IMPORTANCE OF GUT MICROBIOME IN HEALTH

Definition and Overview

An imbalance in the microbial community in our intestines is known as gut dysbiosis, and it can have detrimental effects on our health. The term "gut microbiome" refers to the trillions of bacteria, viruses, fungi, and other microorganisms that live in the human gut. These microbes are essential for immunological response, digestion, and general health [6-7]. A group of disorders known as metabolic syndrome raise the risk of type 2 diabetes, heart disease, and stroke. These disorders include abnormal cholesterol levels, high blood pressure, high blood sugar, and excess body fat around the waist. Serious health issues are more likely to arise when these diseases coexist (Figure 1) [8–10].

The Relationship between Gut and Metabolic Health

Maintaining metabolic health depends on the gut microbiota. Digestion, blood sugar regulation, fat storage, and immune system modulation are all facilitated by a healthy gut flora. These mechanisms are upset by an imbalance called gut dysbiosis, which can result in inflammation, insulin resistance, and other metabolic problems [11-12].

The Importance of the Gut Microbiome

The trillions of microorganisms that live in the human digestive tract, including bacteria, viruses, fungus, and other microbes, make up the complex and dynamic gut microbiome. This enormous microbial community is essential to preserving human health and wellbeing [13]. It affects a number of physiological functions, including immunological response, emotional well-being, digestion, and nutrient absorption.

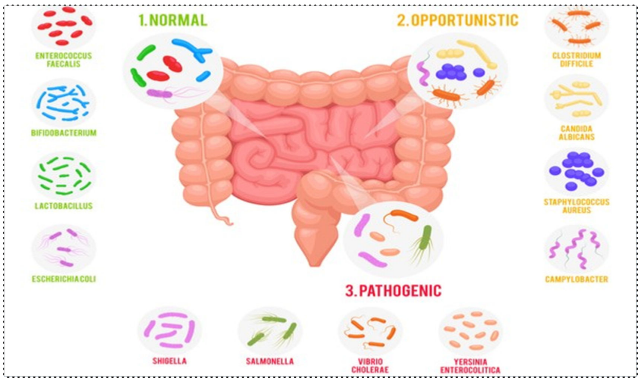


Figure 1: Gut Microbiome in Normal, Opportunistic and Pathogenic State [14]

The Composition and Diversity of the Gut Microbiome

Every person has a different microbial makeup, making the gut microbiome a very diverse environment. Maintaining a balanced and healthy gut environment depends on this diversity. Firmicutes, Bacteroidetes, Actinobacteria, and Proteobacteria are the main phyla of bacteria found in the human gut. A number of variables, including nutrition, genetics, environment, and lifestyle, can affect the relative abundance of these groups [15–18]. Resilience and stability are linked to a diverse gut microbiota, which enables the system to withstand disruptions and adjust to changes. Numerous processes, such as the synthesis of short-chain fatty acids (SCFAs), the metabolism of complex carbohydrates, and immune system regulation, depend on this diversity [19].

Major impact of Gut Microbiome in metabolic Health

- Nutrient Absorption and Metabolism: Aiding in the digestion and absorption of nutrients is one of the gut microbiome's main roles. Our bodies are unable to break down complex proteins, fibres, and carbohydrates without the help of the enzymes produced by the bacteria in our gut. SCFAs including acetate, propionate, and butyrate are produced as a result of this process and are crucial for gut health and energy metabolism (Figure 2) [20-24].

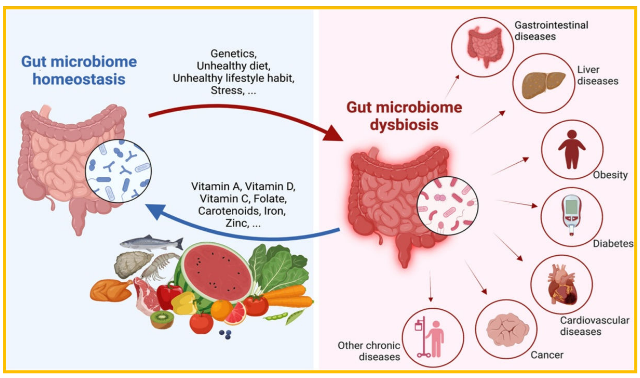


Figure 2: Gut Microbime, dysbiosis and Metabolic diseases [25]

- Complex Carbohydrate Digestion: The enzymes required to break down some complex carbohydrates, such cellulose and resistant starch, are absent from human cells. These enzymes are found in gut bacteria, especially those belonging to the phyla Firmicutes and Bacteroidetes, which aid in the fermentation of these carbohydrates into SCFAs, which give colon cells energy and have anti-inflammatory qualities [26].

- Vitamin Production: Essential vitamins, such as vitamin K and various B vitamins (B12, riboflavin, folate, and biotin), are produced by certain gut bacteria. These vitamins are essential for cellular metabolism, energy synthesis, and blood coagulation [27-30].
- Mineral Absorption: The gut microbiota affects how minerals like calcium, magnesium, and iron are absorbed. For instance, the colon's pH is lowered by SCFAs made by gut bacteria, which improves calcium's solubility and absorption [31-32].
- Immune Function and Protection Against Pathogens: The immune system's growth and operation depend heavily on the gut microbiota. It interacts with the body's major immune system component, gut-associated lymphoid tissue (GALT). Through these interactions, the gut microbiome teaches the immune system to differentiate between benign or helpful microorganisms and dangerous pathogens [33-34].
- Immune System Modulation: Both innate and adaptive immune responses are influenced by the gut microbiota. It increases the generation of regulatory T cells (Tregs) that support immunological tolerance, modifies the activity of immune cells including macrophages and T cells, and boosts the production of antimicrobial peptides [35].
- Barrier Function: The integrity of the gut barrier is maintained by a healthy gut microbiome, which stops toxins and dangerous infections from moving into the bloodstream. SCFAs, especially butyrate, increase the synthesis of tight junction proteins that close the gaps between epithelial cells, strengthening the gut barrier [36-38].
- Pathogen Defense: Pathogenic bacteria and the gut microbiome vie for resources and attachment points on the intestinal lining. Additionally, it generates antimicrobial compounds that stop dangerous bacteria from growing, like bacteriocins and SCFAs.
- Mental Health and the Gut-Brain Axis: Through the gut-brain axis, a two-way communication pathway that connects the enteric nervous system (ENS) of the gut and the central nervous system (CNS), the gut microbiota has a significant influence on mental health. Neural, hormonal, and immunological pathways are involved in this axis, and gut bacteria are crucial in regulating these connections [39-42].

- Neurotransmitter Production: Numerous neurotransmitters that affect mood, anxiety, and cognitive function, including as serotonin, dopamine, and gamma-aminobutyric acid (GABA), are produced and regulated by gut microbes. For example, the gut produces about 90% of the body's serotonin [43-44].
- Inflammation and Mood Disorders: Increased inflammation is associated with gut dysbiosis, or an imbalance in the gut microbiome, and is a risk factor for anxiety and depression. By changing the production of inflammatory cytokines and compromising the blood-brain barrier, chronic inflammation can have an impact on behaviour and brain function [45-46].
- Stress Response: The hypothalamic-pituitary-adrenal (HPA) axis is modulated by the gut microbiota, which affects how the body reacts to stress. It has been demonstrated that some probiotics, referred to as psychobiotics, lessen stress-related behaviours and cortisol levels [47-49].

EVIDENCE CONNECTING DYSBIOSIS, METABOLIC ISSUES AND INTERVENTIONS

Through interprets including energy harvest, inflammation, leaky gut, toxic metabolites, and epigenetic modifications, gut dysbiosis is closely associated with obesity, type 2 diabetes, metabolic syndrome, and related disorders, according to numerous research. Changing the microbiota can enhance metabolic indicators, suggesting a contributing causative role, according to data from animal and early human interventions. However, dysbiosis in humans is best understood as both a cause and an effect of metabolic disease rather than as a single, established root cause. [Table 1 and 2].

Table 1: Important connections between metabolic consequences and dysbiosis.

Findings and Outcome	Summary	Citation
Changes in the microbiota in glucose disorders	Compared to their metabolically healthy counterparts, older persons with prediabetes/T2D have reduced Bacteroidetes and more Erysipelotrichaceae and Lachnospiraceae.	[50]
Common dysbiosis in obesity, T2D and NAFLD	Decreased diversity and distinct patterns of "unhealthy" versus "probiotic" taxa in a number of metabolic illnesses	[51-53]

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Gut dysbiosis & Metabolic Syndrome risk (diet-based index)	Increased dietary index favoring microbiota leads to decreased Cardiovascular mortality and Metabolic Syndrome prevalence.	[54-55]
Dangerous microbiological metabolites	TMAO, LPS, indoxyl sulfate, pcresol sulfate promotes lowgrade inflammation and Metabolic Syndrome characteristics	[56-59]
Endotoxemia and Leaky gut	Dysbiosis leads to endotoxin translocation (also known as "intestinal endotoxemia"), barrier degradation, inflammation, and Metabolic Syndrome.	[60]
Intervention evidence and Transfer	Fecal microbiota transfer or microbiotatargeted therapies can improve insulin sensitivity, weight, lipids in animals and some humans	[61-62]

Table 2: Scientific evidence of dysbiosis and Metabolic Health

Assert	Evidence and Strength	Rationalization	References
Dysbiosis is strongly associated with metabolic disorders	Strong	Many human cohorts, systematic reviews and multiomics studies show consistent associations	[63-66]
Dysbiosis can contribute causally to metabolic dysfunction	Moderate	Animal transfers, human FMT and probiotics/ prebiotics improve metabolic markers, but human causality still debated	[67]
Correcting dysbiosis reliably treats Metabolic Syndrome in humans	Moderate	Metaanalyses show modest but significant improvements; effects vary by intervention, duration, population	[68]

THE GUT MICROBIOME ROLE IN METABOLIC HEALTH AND ENERGY PRODUCTION:

The regulation of metabolic processes, such as the metabolism of lipids and glucose, is largely dependent on the gut microbiota. Metabolic illnesses like obesity, type 2 diabetes, and metabolic syndrome are linked to dysbiosis, or an imbalance in the gut microbiome.

- Energy Harvesting: Some bacteria in the gut are better at obtaining energy from food. By improving the extraction of calories from the diet, a higher concentration of these bacteria can lead to weight gain and obesity [69-70].
- Insulin Sensitivity: By increasing glucose absorption in muscle and adipose tissue and encouraging the secretion of glucagon-like peptide-1 (GLP-1), an incretin hormone that increases insulin release, SCFAs generated by gut bacteria, especially butyrate and propionate, improve insulin sensitivity [70-71].
- Lipid Metabolism: By influencing how lipids are absorbed and stored, the gut microbiota affects lipid metabolism. Changes in bile acid metabolism brought on by dysbiosis may promote the buildup of fat in the liver and adipose tissue [72-73].

GUT DYSBIOSIS AND CHRONIC DISEASES:

Beyond metabolic problems, a number of chronic conditions, such as inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), cardiovascular disease, and autoimmune illnesses, are associated with an imbalance in the gut microbiota. An imbalance between good and bad bacteria in the gut leads to gut dysbiosis. Numerous variables, such as poor food, stress, sleep deprivation, abuse of antibiotics, and certain medical problems, can cause this imbalance. The variety and well-being of gut bacteria can be diminished by a diet heavy in processed foods and low in fibre. Digestive problems like bloating, diarrhoea, constipation, and abdominal pain are common signs of gut dysbiosis, however they can vary greatly. In addition to its effects on the digestive system, gut dysbiosis can lead to mental health issues like anxiety and depression as well as skin disorders like dermatitis.

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- Inflammatory Bowel Disease (IBD): IBD, which includes Crohn's disease and ulcerative colitis, is characterized by dysbiosis. Chronic gut inflammation is generally caused by an overabundance of pro-inflammatory bacteria and decreased microbial diversity in IBD patients (Figure 3) [74-75].
- Irritable Bowel Syndrome (IBS): IBS symptoms like bloating, changed bowel patterns, and abdominal pain are linked to changes in the gut microbiota. These symptoms can be reduced by probiotics and dietary changes that target the microbiome [76].
- Cardiovascular Disease: Dietary nutrients including choline and carnitine are metabolized by gut bacteria to produce trimethylamine-N-oxide (TMAO), a substance associated with a higher risk of cardiovascular disease. Cardiovascular risk can be decreased by lowering the quantity of TMAO-producing bacteria through dietary modifications or probiotics [77-80].

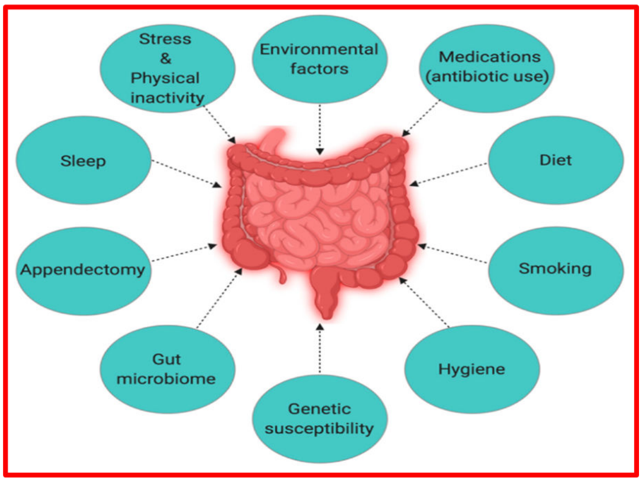

Figure 3: The interplay of factors causing inflammatory bowel disease (IBD) [81]

- Autoimmune Disorders: Rheumatoid arthritis, multiple sclerosis, and type 1 diabetes are among the autoimmune disorders whose development is linked to dysbiosis. Changes in the gut microbiota can cause autoimmune reactions and impair immunological tolerance [82].

KEY CRITERIA'S FOR MAINTAINING A HEALTHY GUT MICROBIOME

Promoting a healthy gut microbiome involves a combination of dietary, lifestyle, and environmental factors. Here are some key strategies:

- Diet: A balanced gut microbiota is supported by a varied diet high in fibre, fruits, vegetables, whole grains, and fermented foods. Limit foods that are heavy in sugar, harmful fats, and refined carbohydrates.
- Probiotics and Prebiotics: Gut health can be improved by consuming probiotics, which are good bacteria, and prebiotics, which are fibres that support good bacteria. Good sources include fermented foods like yoghurt, kefir, sauerkraut, and kimchi, as well as probiotic pills.
- Avoiding Unnecessary Antibiotics: By eliminating helpful bacteria, antibiotics can alter the gut microbiota. They should only be used as directed by a medical professional and when absolutely required.
- Managing Stress: The gut microbiome can be adversely affected by long-term stress. Stress-reduction techniques include regular exercise, meditation, and mindfulness.
- Adequate Sleep: A healthy gut microbiome depends on getting enough sleep. Inadequate sleep habits can lead to gut dysbiosis and disturb the microbial equilibrium.
- Regular Exercise: By boosting microbial diversity and bolstering gut barrier function, physical activity supports a healthy gut microbiome [83].

METABOLIC SYNDROME EXPLAINED:

When at least three of the following risk factors are present, metabolic syndrome is diagnosed: Together, they result in low HDL cholesterol, high triglyceride levels, elevated waist circumference (abdominal obesity), Elevated blood pressure and elevated fasting blood glucose levels [84-88].

- Risk Factors and Prevalence: Genetic predisposition, poor diet, inactivity, and certain medical diseases like fatty liver disease and polycystic ovarian syndrome (PCOS) are risk factors for metabolic syndrome. Globally, metabolic syndrome is becoming more common due to increased obesity and sedentary lifestyle rates.
- Health Implications and Long-term Effects: The risk of type 2 diabetes, cardiovascular disease, and other major illnesses is greatly increased by metabolic syndrome. Long-term consequences include higher healthcare expenses, a decline in quality of life, and an increase in mortality.
- Link Between Gut Dysbiosis and Metabolic Syndrome: Metabolic syndrome can be exacerbated by gut dysbiosis in a number of ways. Increased gut permeability, or "leaky gut," can result from an unbalanced gut flora, allowing toxic chemicals to enter the bloodstream and cause inflammation. Insulin resistance and other elements of the metabolic syndrome are largely caused by chronic inflammation.
- Role of Inflammation and Immune Response: A key factor in the connection between intestinal dysbiosis and metabolic syndrome is inflammation. Endotoxins from gut bacteria can enter the bloodstream and trigger an immunological response when the gut barrier is breached. Metabolic syndrome may occur as a result of this persistent, low-grade inflammation that interferes with metabolic functions.
- Impact on Metabolism and Insulin Sensitivity: The way the body absorbs and stores nutrients is influenced by gut flora. Short-chain fatty acids (SCFAs), which are involved in controlling metabolism and insulin sensitivity, can be produced differently as a result of dysbiosis. Reduced SCFA production from a disturbed gut flora can hinder the metabolism of fat and glucose and increase insulin resistance.

DIAGNOSIS, IDENTIFICATION AND INTERVENTIONS FOR GUT DYSBIOSIS:

In addition to laboratory testing to determine the makeup of gut bacteria, the diagnosis of gut dysbiosis usually entails a review of symptoms and medical history. To find microbial imbalances and direct treatment, stool testing is frequently utilized. Since there are no particular tests to identify gut dysbiosis, doctors may use pathology and screening testing to rule out other structural illnesses [89-91].

- Probiotics: Types, Sources, and Benefits: When taken in sufficient quantities, probiotics live bacteria offer health advantages. Supplements and fermented foods including yoghurt, kefir, sauerkraut, and kimchi contain them. Probiotics boost metabolic health, lower inflammation, and re-establish a balanced population of gut flora

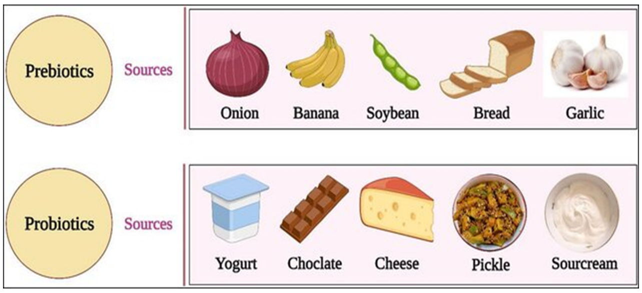

Figure 4: Source of pre and Probiotics [92]

- Prebiotics: Types, Sources, and Benefits: Beneficial gut bacteria are fed by prebiotics, which are indigestible fibres. Garlic, onions, leeks, asparagus, bananas, and whole grains are examples of common prebiotic foods. Prebiotics improve the function of the gut barrier, encourage the growth of beneficial bacteria, and support gut health in general.
- Dietary Changes: Foods to Include and Avoid: Fibre, fruits, vegetables, whole grains, and lean meats are all important components of a diet that promotes intestinal health. Limit foods that are heavy in sugar, harmful fats, and refined carbohydrates. A healthy gut microbiome can be maintained by consuming fermented foods and meals high in fibre.
- Fecal Microbiota Transplantation (FMT): Procedure and Efficacy: Faecal matter from a healthy donor is transplanted into the gut of a dysbiosis patient as part of FMT. A balanced microbial population can be restored with the aid of this process. FMT is being investigated as a treatment for metabolic syndrome and has demonstrated promise in treating a number of ailments, such as inflammatory bowel disease and recurrent Clostridium difficile infections.
- Emerging Therapies and Research: New therapies for gut dysbiosis are being developed, including targeted probiotics, microbiome-based drugs, and personalized nutrition plans. Ongoing research aims to better understand the gut microbiome's role in health and disease and to develop more effective interventions. Special attention is required to treat Gut dysbiosis by several biomedical options [93]. The therapeutic options are broadly divided into the following categories:
  - o Medicinal treatment,
  - o Bacterial supplementation.
  - o Medicinal management is required and consists of desorption of gut toxins,
  - o controlling hypermotility using anti- peristaltic therapy,
  - o bicarbonate neutralization of hydrogen gas in case of SIBO,
  - o probiotics,
  - o antimicrobials,
  - o reabsorption of bile acids
  - o gas production inhibitors.
- Daily Habits and Lifestyle Changes: A balanced diet, regular exercise, enough sleep, and stress reduction are all necessary to maintain gut health. A healthy gut microbiota can be maintained by include a range of plant-based diets, drinking plenty of water, and avoiding needless antibiotics.
- Importance of Regular Check-ups and Monitoring: Monitoring metabolic risk factors and intestinal health might be facilitated by routine examinations with medical professionals. The prevention and management of metabolic syndrome depend heavily on early detection and intervention.

ONGOING RESEARCH AND FUTURE DIRECTIONS

The study of the gut microbiome and how it affects metabolic health is developing quickly. Future directions include the investigation of novel microbial medicines and the creation of customized treatments based on each person's own gut microbiota. The advancement of personalized medicine is closely linked to the growing number of illnesses linked to gut dysbiosis. As the relationship between the gut microbiome and diseases is further investigated, research hotspots in health issues based on the regulation and intervention of the gut microbiome can be predicted from a variety of multi-dimensional perspectives, including the general overview, in-depth analysis by category and field, and relationship analysis of keywords. Gut dysbiosis is known to have a major impact on a number of diseases, including metabolic syndrome, cardiovascular disease, inflammatory bowel disease, cancer, and neurological disorders. These illnesses pose a major threat to people's health. In the era of precision medicine, treatments or interventions can be customized for each patient based on their particular illness characteristics.

Critical discussion

Dysbiosis promotes obesity, insulin resistance, dyslipidaemia, hypertension, and fatty liver via increasing reactive oxygen species, inflammation, intestinal permeability, and epigenetic alterations. Changes in energy extraction, metabolism of carbohydrates, disturbance of the intestinal barrier, immunological activation, metabolism of bile acids, and microbial metabolites (particularly short-chain fatty acids) are important processes. Type 2 diabetes, Open Access Freely Availiable Online

metabolic syndrome, and obesity are frequently linked to decreased microbial diversity and compositional changes. Many relationships are correlative, and processes and causality are still poorly understood. Inconsistent results are caused by train-specific effects, varying dosages, durations, endpoints, and mixed animal/human data. Significant variations in the microbiome between individuals and contexts make standardization and generalization difficult. Precision and personalized methods: combining genetics, metabolomics, and machine learning with microbiome data to customize therapies. Deeper analysis of host-microbe pathways, such as microbial carbohydrate metabolism, particular metabolites, and epigenetic impacts, is possible through mechanistic and multi-omics study. Determining strong biomarkers and essential taxa/functions for metabolic health and recovery from dysbiosis is the definition of resilience and "healthy" microbiomes. Extended, superior clinical trials: standardized, independently financed Randomized Controlled Trials (RCTs) with sufficient follow-up to evaluate the safety and long-term metabolic benefits of microbiome-targeted treatments. Gut dysbiosis is not merely a bystander to metabolic illnesses; it is a changeable factor. Dietary patterns, pre/pro/syn/postbiotics, and FMT are examples of microbiome-targeted therapies that can supplement lifestyle and pharmaceutical therapy. Probiotics/synbiotics and dietary fiber-rich interventions have the best current evidence for improving glucose and lipid profiles. Personalized strategies, reliable biomarkers, and integration into multidisciplinary metabolic illness treatment frameworks will probably be necessary for translation into routine care.

CONCLUSION

The development of metabolic syndrome, a group of disorders that raise the risk of heart disease, diabetes, and other health issues, is significantly influenced by gut dysbiosis, an imbalance in the gut microbiome. Maintaining metabolic health requires a healthy gut microbiota since it is vital for immunological response, energy metabolism, and nutrition absorption. Dietary modifications, such as consuming more fibre and probiotic-rich fermented foods, as well as avoiding overuse of antibiotics, are interventions to treat gut dysbiosis. A balanced gut microbiome is also influenced by lifestyle changes like consistent exercise, stress reduction, and enough sleep. We can lower the incidence of metabolic syndrome and enhance general health by realizing the significance of the gut microbiota and taking action to support its health. Research in this area will continue to offer insightful information and fresh approaches to controlling and preventing metabolic syndrome through gut health.

Author contribution

It is hereby acknowledged that all authors have accepted responsibility for the manuscript's content and consented to its submission. They have meticulously reviewed all results and unanimously approved the final version of the manuscript.

Consent for publication

Not applicable

CONFLICT OF INTEREST

The author declares no conflicts of interest.

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