WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 14, Issue 10, 393-397. Review Article ISSN 2277–7105

GUT-MICROBIOME DYSREGULATION AS THE MAJOR RISK FACTOR IN OBESITY

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Article Received on
28 March 2025,

Revised on 18 April 2025,
Accepted on 08 May 2025

DOI: 10.20959/wjpr202510-36678

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ABSTRACT

Most recently, scientific research has dramatically shifted our understanding of the root causes of obesity. Traditionally, this metabolic disorder has been seen primarily through the lens of genetics, lifestyle choices, and environmental factors such as diet and physical inactivity. However, a growing body of evidence suggests that there is another key player in the obesity epidemic that has been largely overlooked: the gut microbiome. The trillions of bacteria, viruses, fungi, and other microorganisms that inhabit our gastrointestinal tract play a crucial role in regulating metabolism, immune function, and energy balance. Studies have demonstrated that certain gut bacteria are linked to metabolic disorders and obesity. For instance, individuals with a higher ratio of *Firmicutes* to *Bacteroidetes* F/B ratio, bacteria in their gut were more likely to be associated with obese individuals. The presence of *Firmicutes* was associated with a 20% increase in calorie absorption from food. Additionally, specific bacteria such as *Proteobacteria* have been consistently reported as obesity-associated. *Prevotella spp*. and, *Roseburia spp*. are butyrate producers; improve insulin sensitivity, in diabetic and obese individuals, *Bacteroidetes*-inversely correlate with BMI, *Clostridium spp.* promotes inflammation and gut permeability, further, *Enterobacter spp*., are endotoxin producers; contribute to systemic inflammation in obese and diabetic individuals.

When this delicate microbial ecosystem becomes dysregulated, it may become a significant driver of obesity. Lifestyle choices and environmental factors indeed play a significant role in

shaping our gut microbiome. Factors such as diet, physical activity, stress levels, and exposure to pollutants can all influence the balance of gut bacteria. For instance, a diet high in processed foods and low in fiber can negatively impact gut health, while regular exercise and a balanced diet rich in fruits, vegetables, and whole grains can promote a healthy microbial ecosystem.

The human gut microbiome is a complex and dynamic community of microorganisms that outnumber human cells by ten to one. These microbes are involved in a wide range of biological processes that are essential for health. They help digest food, produce vitamins, break down toxins, and regulate the immune system. Importantly, they also influence how the body processes energy. The gut microbiome can affect the efficiency of energy absorption from food and even how fat is stored within the body. Studies have shown that obese individuals tend to have a less diverse gut microbiome compared to their lean counterparts. This dysbiosis, or microbial imbalance, is often marked by a higher abundance of certain bacterial species that are linked to inflammation and metabolic dysfunction. One of the most significant discoveries in this field is the way gut bacteria influence the breakdown of dietary fibers. Certain microbes are adept at fermenting fiber into short-chain fatty acids (SCFAs), which are beneficial to human health. These SCFAs not only provide an energy source for the body but also promote the feeling of fullness, helping to regulate appetite and prevent overeating.

Gut-Microbiome Dysregulation and Obesity

The gut microbiome dysregulation can lead to a cascade of metabolic disturbances that contribute to obesity. When the gut microbiome is unbalanced, it can influence the body's insulin sensitivity, fat storage mechanisms, and appetite regulation. One major mechanism through which dysbiosis promotes obesity is through inflammation. It is essential to delve into the specific mechanisms by which gut bacteria influence metabolic disorders and obesity. For instance, certain gut bacteria can extract more calories from food, leading to increased energy absorption and storage. Additionally, these bacteria can produce metabolites that affect insulin sensitivity and fat storage. By understanding these mechanisms, we can better appreciate the complex relationship between gut microbiota and metabolic health. Gut bacteria play a pivotal role in maintaining the integrity of the intestinal lining, which acts as a barrier to prevent harmful substances from entering the bloodstream. In dysbiosis, this barrier can become compromised, allowing toxins, inflammatory molecules, and bacteria to leak into the body—a phenomenon known as "leaky gut." This triggers systemic inflammation, which disrupts normal metabolic processes and can lead to insulin resistance, a precursor to obesity and type 2 diabetes. Additionally, gut dysbiosis can influence the central nervous system. The gut-brain axis, a bi-directional communication pathway between the gut and the brain, allows microbes to send signals that affect appetite and food preferences. In states of dysbiosis, these microbial signals can alter the way the brain processes hunger cues, leading to overeating and cravings for high-calorie, nutrient-poor foods. The F/B ratio is not a definitive diagnostic tool but acts as a biomarker of gut dysbiosis.

Given the strong link between gut-microbiome dysregulation and obesity, scientists are exploring various interventions to restore a healthy microbiome and mitigate obesity risk. Probiotics, prebiotics, and fecal microbiota transplants are some of the strategies under investigation. Probiotics, which contain live beneficial bacteria, have shown promise in improving gut health, but their effectiveness in long-term weight management is still being studied. Prebiotics, on the other hand, are dietary fibers that promote the growth of beneficial microbes, and research has shown that increasing prebiotic intake can help improve gut microbial composition and support weight loss. However a detailed analysis of the mechanisms, effectiveness, and limitations of these alternative options is crucial. For instance, certain gut bacteria can extract more calories from food, leading to increased energy absorption and storage. Additionally, these bacteria can produce metabolites that affect insulin sensitivity and fat storage. By understanding these mechanisms, we can better appreciate the complex relationship between gut microbiota and metabolic health. LPS (lipopolysaccharide)-producing bacteria like *Enterobacter* or *Desulfovibrio* increase metabolic endotoxemia, triggering low-grade chronic inflammation seen in obesity and T2DM.

Gut-microbiome dysregulation has emerged as a major risk factor in obesity, highlighting the importance of looking beyond traditional causes such as diet and physical activity. As research continues to unravel the complex relationship between the gut and metabolism, it is clear that the health of our microbiome is an essential component of our overall well-being. Restoring balance to the gut microbiome could become a key strategy in preventing and treating obesity, offering new hope for individuals struggling with this chronic condition. Just as the microbiome plays a foundational role in health, its role in obesity could reshape the future of obesity management, offering more precise, effective, and holistic interventions. By understanding the unique microbiome composition of an individual, healthcare providers may one day be able to tailor dietary recommendations to restore microbial balance and optimize metabolic health. Dietary interventions can alter the gut microbiome composition, but their effectiveness may vary based on individual differences and adherence to the diet. Similarly, probiotics can introduce beneficial bacteria, but their impact may be limited by the existing microbial ecosystem and the specific strains used. These aspects, can offer a more nuanced understanding of the potential and limitations of these alternatives. This could revolutionize the way obesity is treated, shifting from a one-size-fits-all approach to a more personalized, microbiome-cantered model.

Further reading

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