

Gut dysbiosis and obesity: a systematic review

Abstract

Objective: The aim of this study is to evaluate the existing evidence on the relationship between gut dysbiosis and comorbidities associated with obesity, with a focus on intestinal microbiota and leaky gut syndrome.

Methodology: A search for scientific articles was conducted, with an emphasis on reviews and systematic reviews, using PubMed as the database source. The following terms were considered in the search: “intestinal dysbiosis AND obesity,” which yielded 940 studies. The period from 2013 to 2023 was then defined, resulting in a reduction to 921 studies. Upon selecting full-text studies that were freely accessible, 551 studies were found for analysis. Further refinement by selecting the types of texts (review and systematic review) reduced the number to 245 articles. Ultimately, 39 studies were selected based on their titles. Finally, 11 studies were chosen for comprehensive analysis, focusing on those deemed most relevant to the proposed discussion, which is the connection between the microbiome and metabolic disorders such as obesity.

Results: The results suggest a relationship between intestinal microbiota and the development of obesity, including its complications. Gut dysbiosis has an inflammatory and immunomodulatory effect, leading to insulin resistance and diabetes. Early interventions in the microbiota show a positive effect on dysbiosis as well as leaky gut syndrome, significantly contributing to the treatment of obesity and metabolic disorders.

Conclusions: In summary, the intestinal microbiome proves to be an important component of metabolic processes. It demonstrates a positive effect on reshaping the intestinal microbiota to control body adiposity, improve insulin sensitivity, and achieve other metabolic changes related to obesity.

Keywords: obesity, intestinal microbiota, gut health, metabolic profile, diabetes melitus

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Introduction

The human intestine consists of a symbiosis of over 100 trillion microorganisms that form a community known as the microbiota. The quantity and quality of the species participating in this community have proven to be a determining factor in the incidence of various pathologies, ranging from autoimmune complications to neurobehavioral disorders. The disorder characterized by an imbalance in this microbiota is intestinal dysbiosis, which can have several causes for its occurrence.¹ According to Almeida et al.,² excessive inappropriate treatments affecting the intestine disrupt the balance of the intestinal microbiota, resulting in an increase in harmful bacteria and dysbiosis.² Evidence demonstrates that dysbiosis characterized by low microbial diversity has strong associations with overweight and obesity.¹ This is because an increase in intestinal permeability syndrome and irritable bowel syndrome, which involve microbiome disharmony, can impair the normal functionality of the colon, thus compromising an individual's health.³

The increasing incidence of this disorder, characterized by excess body fat, raises concerns and is already considered a pandemic by the World Health Organization (WHO), which estimates that there will be one billion obese people worldwide by 2030. Obesity compromises human health to such an extent that it causes metabolic, respiratory, and locomotor impairments, and becomes a risk factor for various other diseases.⁴ Furthermore, according to the 2023 Obesity Atlas released by the World Obesity Federation, this problem goes beyond aesthetics and significantly impacts individual health, quality of life, public issues, and the economic sector.⁵ There is a great deal of fallacy surrounding this panorama, both regarding the factors involved in the process of excessive weight gain and its loss. Therefore, further

in-depth research is needed, and promising results regarding the intestinal microbiota seem to play a role in the pathophysiology of this phenomenon. This review aims to analyze the interaction between intestinal dysbiosis and obesity. It seeks to demonstrate the existing relationship between dysbiosis and the comorbidities associated with obesity, and to determine the level of association with the development of obesity, including its complications.

Material and methods

To discuss the composition of the intestinal microbiota in obese individuals, we conducted a literature review that included relevant thematic review and systematic review studies. Exclusion criteria were applied to restrict the analyzed studies to the proposed topic and minimize potential biases and associations with other comorbidities. Initially, a literature search was conducted on the PUBMED database using the keywords: “intestinal dysbiosis AND obesity.” Only studies published between 2013 and 2023 and accessible as full-text were considered for this review.

Furthermore, for methodological quality, the following PICOT strategy was employed in the proposed search: Population - individuals with intestinal dysbiosis, Intervention - the impact of dysbiosis on the incidence of obesity, Control - individuals without dysbiosis, Outcome - dysbiosis as a risk factor for obesity, and Type of text - review and systematic review. Therefore, the analyzed studies were restricted to those relevant to dysbiosis and obesity, excluding those related to other diseases, animals, as well as studies involving children, pregnant women, or lactating women. Finally, following the presented analysis, 11 relevant studies on the topic were selected for further reading, as shown in the attached image (Figure 1).

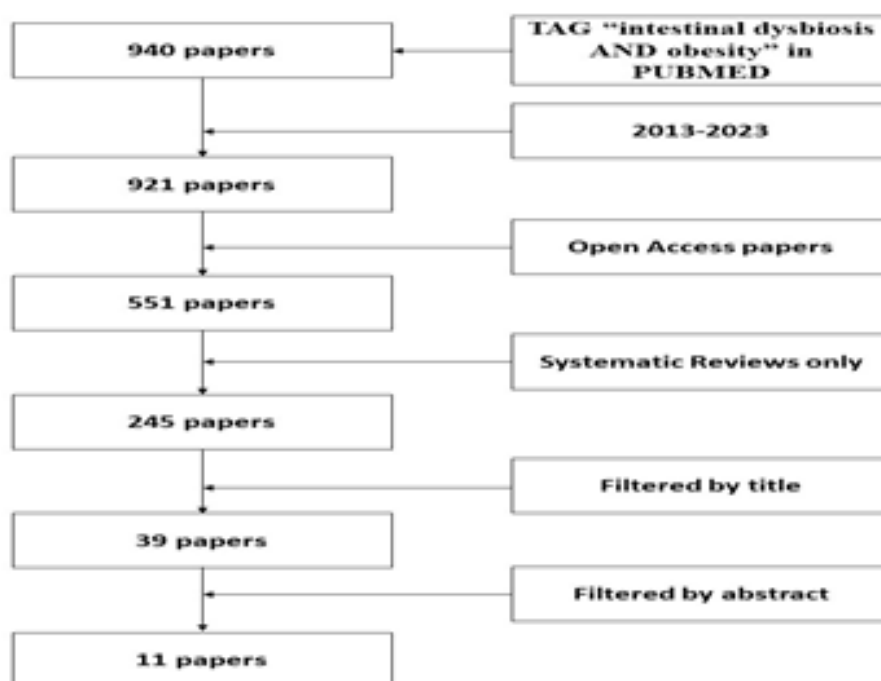


Figure 1 Studies selected for research composition.

Results and discussion

It is the symbiotic relationship, especially regarding the intestinal microbiota, that supports human health and well-being. Thus, considering the diversity, stability, resilience, and symbiotic interaction with the host, as mentioned above, the human being and the microorganisms that inhabit it can be defined as a “superorganism”.⁶ In this relationship, it is noteworthy that the intestinal microbiota has a unique profile for each individual, consisting of different species of bacteria. According to Stojanov et al.,⁷ the most important bacterial phyla for maintaining host homeostasis are Firmicutes and Bacteroidetes.⁷ Therefore, it is important to maintain a balanced ratio between these two phyla in order to promote health. In the analysis of the selected studies, the existence of a relationship between the intestinal microbiota and the development of obesity, including its complications, was found. Some studies have shown that the ratio of Firmicutes to Bacteroidetes is related to obesity. The first study analyzed observed that a higher ratio of Firmicutes to Bacteroidetes is associated with obesity.⁸ This same study suggests that despite heterogeneity in the data, it can be concluded that obesity is associated with intestinal dysbiosis, which alters the functioning of the intestinal barrier, allowing the passage of unwanted components such as bacteria. These issues lead to an inflammatory profile that can contribute to the development of insulin resistance.

Supporting the above results, Stojanov et al.,⁷ observes that an increase in the Firmicutes/Bacteroidetes ratio is associated with obesity development. Therefore, dietary supplements and probiotics that can contribute to the restoration of this ratio are suggested as a means of treating or preventing obesity.⁷ Another study relates lower energy expenditure and higher caloric intake to an increase in the Firmicutes phylum, resulting in weight gain and obesity due to fat accumulation in the host’s tissue.^{9,10} This same article states that there is a correlation between obesity and a 50% decrease in the Bacteroidetes-to-Firmicutes ratio. Another author suggests that the obese gut microbiota has a lower quantity of Bacteroidetes division

members and a higher quantity of Firmicutes division members.¹¹ Furthermore, a study confirms the impact of microbial composition on metabolic disorders: “Many studies in animals and humans have shown differences in body weight between organisms with different compositions of the gut microbiota. The greatest impact was demonstrated in changes in the Bacteroidetes/Firmicutes ratio and the involvement of *Lactobacillus*. However, many other bacterial genera in the gut microbiota seem to be associated with a tendency to develop obesity”.¹² On the other hand, Magne et al.,¹³ state that “the relative abundance of the Firmicutes and Bacteroidetes phyla is highly variable among individuals of the same population”.¹³ This is likely due to many factors... Although the gut microbiota may contribute to the development of obesity, the evidence suggesting an association between obesity and alterations in the Firmicutes/Bacteroidetes ratio is not convincing, highlighting the need for further studies to draw more conclusive evidence. Tokarek et al.,¹² highlight the important role of Short-Chain Fatty Acids (SCFA) absorbed or excreted in feces, derived from the metabolism of dietary fibers, in maintaining proper body weight. Furthermore, according to the Obesity and Eating Habits Research Center (2020), in their study “Gut microbiota-derived metabolites in obesity: a systematic review,” intervention studies aimed at modulating the intestinal microbiota and consequently the metabolic profile in obesity can also contribute to obesity control.⁵ Another study also suggests that the treatment of obesity may be directly linked to the improvement of the intestinal microbiota in obese individuals.¹⁴ In line with the study “Gut microbiota-derived metabolites as key mucosal barrier modulators in obesity” by Wei et al., the intestinal microbiota plays an essential role in obesity, and the use of microbes and their metabolites in the gut represents promising new and safe therapeutic modalities for metabolic diseases.¹⁵ Finally, the study “Gut Microbiota Interventions for the Management of Obesity: A Literature Review” by Gill et al.,¹⁶ demonstrated that microbial manipulation can be employed to prevent or treat weight gain and associated comorbidities. In other words, by treating the intestinal microbiota, we can control obesity (Table 1).^{16,17}

Table 1 Analysis of eligible articles from the review study

Author/year	Target	Findings	Conclusion
Gomes et al. ⁸ 2018	Discussing the composition of the intestinal microbiota in obese individuals.	A higher ratio of Firmicutes to Bacteroidetes is associated with obesity. Additionally, the Firmicutes phylum has been shown to be negatively correlated with resting energy expenditure (REE) and positively correlated with body fat percentage.	1) Obesity was characterized by the presence of intestinal dysbiosis, marked by a distinct microbiome profile existing between obese and non-obese individuals. 2) The resulting dysbiosis could alter the functioning of the intestinal barrier and gut-associated lymphoid tissue (GALT), allowing the passage of structural components of bacteria, such as lipopolysaccharide (LPS), and activating inflammatory pathways that may contribute to the development of insulin resistance through the alteration of insulin receptor signaling by the presence of inflammatory cytokines. 3) Intestinal dysbiosis could alter the production of gastrointestinal peptides related to satiety, resulting in increased food intake and contributing to a self-sustaining cycle.
Stojanov et al. ⁷ 2020	To summarize the properties of the two most important bacterial phyla found in the intestine, Firmicutes and Bacteroidetes, and their role in maintaining host homeostasis. A balanced ratio between these two phyla is important for maintaining health, and alterations in the ratio are associated with the development of intestinal dysbiosis and certain diseases, such as obesity and DM-II.	An increase in the Firmicutes to Bacteroidetes ratio is associated with obesity. Manipulating the intestinal microbiota with different dietary supplements can contribute to the restoration of the dysbiotic Firmicutes to Bacteroidetes ratio and the treatment or prevention of obesity. Consumed through food or supplements, probiotics can influence the intestinal microbiota and reduce obesity.	Increased or decreased Firmicutes to Bacteroidetes ratios are associated with the development of obesity or diabetes mellitus type II (DM-II), respectively. Overall, the selected probiotics can impact Firmicutes to Bacteroidetes dysbiosis and contribute to the reduction of obesity and intestinal inflammation.
Machate et al. ⁹ 2020	Highlight the interaction between the intake of fatty acids (FA) and the composition of the intestinal microbiota and its interaction with hosts in promoting health and preventing obesity and related metabolic dysbiosis.	Different types of dietary intake of FA play a crucial role in modifying the composition of the intestinal microbiota, which interacts with the improvement of the host's health or disease.	The consumption of high fat diet (HFD), including a low-fat diet with long chain fatty acid (LCFA) intake, increases the beneficial microbiota, mainly the ratio of Bacteroidetes to Firmicutes, as well as species of Actinobacteria and Proteobacteria..
Magne et al. ¹³ 2020	Show the relevance of the Firmicutes/Bacteroidetes ratio to intestinal dysbiosis in obese patients.	The relative abundance of the Firmicutes and Bacteroidetes phyla is highly variable.	The relative abundance of the Firmicutes and Bacteroidetes phyla is highly variable.
Mitev K, Taleski V et al., ¹¹ 2019	Provide an overview of the possible associations between gut microbiota and obesity.	The Firmicutes/Bacteroidetes ratio is altered by obesity and weight loss.	The microbiota of obese individuals has a higher capacity to extract energy. The gut microbiota affects appetite and energy balance. Lifestyle and diet influence the diversity of the microbiota and the presence of dysbiosis.
Tokarek et al., ¹² 2022	Investigate the impact of gut microbiota on the prevalence of obesity and associated morbidities.	Difference in body weight among organisms with different composition of gut microbiota.	The microbiota plays a vital role in the prevalence of obesity.
Vidal et al., ¹⁴ 2016	Associate intestinal microbiota as a contributing factor to obesity.	Synthesize various information related to microbiota and obesity and accelerate the future discovery of new therapeutic applications..	Identify different bacterial phyla involved in obesity, and the treatment of obesity can be achieved through the modification of the microbiota of obese individuals. This process can be accomplished through the transplantation of a known microbiota that is not associated with obesity.
Gill et al., ¹⁶ 2022	How interventions in the intestinal microbiota can control obesity	There is a great heterogeneity in the available data on the subject, and the conclusion that can be drawn from the literature review is that dysbiosis can alter the functioning of the intestinal barrier.	Understanding the changes that occur in the microbiota of obese individuals and the physiological consequences of these changes is a necessary step in the development of future modulation strategies and is a potential area for future research.
Wei et al., ¹⁵ 2021	Microbiota-derived metabolites as key modulators of the mucosal barrier in obesity.	The intestinal microbiota plays a fundamental role in obesity. Our current understanding of host-microbiota interactions remains in its early stage.	The design and use of microbes and their locally active metabolites in the intestine, without systemic side effects, are promising new and safe therapeutic modalities for metabolic diseases.
Ejtahed et al., ¹⁷ 2020d	Analyzing metabolites derived from the gut microbiota in obesity.	An overview of the role of metabolites derived from the gut microbiota in obesity, where these metabolites can impact various metabolic pathways in the host, leading to obesity.	There is no consensus on which type of intervention to modulate the gut microbiota will induce a better metabolic profile in obesity. More studies are needed in this field to develop strategies for modifying specific gut microbiota-derived metabolites.

Conclusion

Considering mentioned findings, it can be observed that the intestinal microbiota is directly related to the treatment of comorbidities associated with overweight and obesity. Obesity cases are predominantly associated with intestinal dysbiosis, making it one of the main approaches to treat these conditions.

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None.

Conflicts of interest

The authors declare no conflicts of interest regarding the research and findings presented.

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