

Microbiome

Role and functionality in human nutrition cycle

Fahad Alhusain, MSc.

ABSTRACT

توجد الميكروبات في كل مكان تقريباً على هذه الأرض. حيث تستوطن الميكروبات في أعضاء مختلفة من جسم الإنسان، بما في ذلك الجلد والأمعاء والفم والأنف. من بين تلك الأعضاء، منطقة الأمعاء. حيث تحوي على أكبر عدد من الميكروبات. ترتبط جراثيم الأمعاء ارتباطاً مباشراً بالحفاظ على استقرار الجسم، ويؤدي التغيير الطفيف في أعدادها إلى تعريض الإنسان للأمراض. والجدير بالذكر أن دور الميكروبات في الجهاز الهضمي يساهم بشكل مباشر في وزن الجسم. حيث أنه في بعض الأحيان ترتبط التغييرات في نمط الحياة أو تناول المضادات الحيوية، لعلاج بعض أنواع العدوى، باضطراب في البكتيريا المعوية. تشير العديد من الدراسات العلمية إلى ارتباط السمنة بالميكروبات المعوية. تركز هذه المراجعة بشكل أساسي على كيفية مساهمة التغذية الصحية في الحفاظ على الميكروبات المعوية النافعة داخل جسم الإنسان. الأهم من ذلك تمت مناقشة مساهمة البروبيوتيك والبريبايوتكس في الحفاظ على وزن الجسم الصحي.

Microbes are present almost everywhere on this Earth. Humans harbor microbes in various organs, including skin, gut, mouth, and nose. Among these, the gut region has the highest population of microbes. Gut microbiota is directly linked with homeostasis, and a minor change in their numbers predisposes humans to ailments. Notably, the role of the microbial population in the digestive tract directly contributes to body weight. Sometimes, lifestyle changes or antibiotics intake to manage certain infections are associated with disturbance in the gut microflora. Several scientific studies allude to the obesity linkage with disturbed intestinal microflora. This review mainly focuses on how healthy nutrition contributes towards maintaining normal flora inside the human body. Importantly, the contribution of probiotics and prebiotics in maintaining human healthy body weight is discussed.

Keywords: gut, microbiota, bariatric surgery, obesity, probiotics

*Saudi Med J 2021; Vol. 42 (2): 146-150
doi: 10.15537/smj.2021.2.25587*

From the Scientific Research Center, Prince Sultan Military Medical City, Riyadh, Kingdom of Saudi Arabia.

*Address correspondence and reprint request to: Fahad Alhusain, Scientific Research Center, Prince Sultan Military Medical City, Riyadh, Kingdom of Saudi Arabia. E-mail: Fahad.rmh@gmail.com
ORCID ID: <https://orcid.org/0000-0002-5062-9750>*

Normal microbiota refers to the micro-organisms colonizing specific organs of the human body and contributing toward bodily homeostasis. Importantly, a wider microbial diversity has been reported within one body organ compared with others.¹ The presence of microbial population has been reported almost in every organ, including the nose, mouth, ears, and so on; however, relatively gut has the highest population with a broader diversity of microbial population.² The outcome of the interactions between the colonization of normal microbiota and the human body has important implications. Normal microbiota in humans plays an essential role in catabolism and the assimilation of food. Therefore, gut microbiota continuously contributes to digestion by enzymatically fermenting carbohydrates, fatty acid production from complex fats, which is then absorbed by the cells of the digestive tract. Besides contributing to the digestion process, gut microbiota compete with pathogenic microbes besides triggering the immune system to kill pathogens.³ Through fermentative processes, microbes aids in the digestion of food and the absorption of beneficial nutrients.⁴ It has also been observed that some naturally occurring microbiota (in the form of opportunistic microbes) can cause infection or other host diseases. One such disorder is the pathogenic cascade leading to obesity. Among several other, one possible reason behind this phenomenon may be gut microbiota.⁵

This review aims to explore microbiota's role in human nutrition and how the disruption in the number and species of normal gut flora can lead to obesity. It has been divided into 5 parts. It begins with a short introduction to normal microbiota in the human

body, emphasizing the physiological microbiota of the human gut. Secondly, we describe how food can affect the number and diversity of gut microbiota. The third section presents the impact of gut microbes on human metabolism and environments, leading to obesity. A comparison of gut microbiota between normal and obese individuals is also described in this section. The fourth section describes explicitly how bariatric surgery can affect normal microbiota. Finally, we put forward avenues for further research that could lead to possible treatment strategies for obesity.

Gut microbiota. The human gut has a diversity of microbes based on the availability of nutrients in a particular region. For example, mono, disaccharide, and amino acids are abundantly present in the smaller intestine, the primary nutrients favoring the growth of lactobacilli and proteobacteria.⁶ Among vertebrates, including humans, the microbes start colonizing the gut in earlier days. The microbial population has been reported to get diversified with antibiotics, environments in different regions of the world, and feeding, namely, breast versus formula milk. Although gut microbiota is highly sensitive and changes in health in disease conditions, the newborn's earlier 3 years are crucial in defining the gut microflora and their diversity.⁷ To understand the mechanism of how microbes, colonize the gut, it is critical to know how the human body is exposed to microbes during infancy. Infants are exposed to microbes through 2 main pathways. The first interaction is during the process of delivery through the mother's vaginal microbial population. Importantly, newborns through normal delivery are quite different from those delivered through cesarean as far as their gut microbiome is concerned.⁸ The second interaction is during breastfeeding.⁹ Thus, these 2 mechanisms initiate the primary inhabitancy of facultatively anaerobic proteobacteria in the gut. These proteobacteria then modify the gut environment by changing the concentration of oxygen. This leads to other species' growth, which could colonize the gut, such as bacteroides and firmicutes. Eventually, many other species find their place and colonize in a healthy human gut, forming normal gut microbiota. Metagenomics studies of the gut microbiome have been crucial in identifying their diversity. The microbial communities in the human gut fall into 3 major groups: eukaryota, archaea, and bacteria. There are significant

differences in the microbiota communities, depending on the environment of the residing region of the gut.¹⁰ These environmental variations of different areas are based on factors like pH and concentration of oxygen. The gut is divided into 3 main areas: stomach, small intestine, and large intestine. The stomach is likely to have a lower number of microbes due to acidic pH. However, some microbes can live and survive in this environment, such as *Streptococcus*, *Staphylococcus*, *Lactobacillus*, *Peptostreptococcus*, and yeast-like candida. Relatively, proportion of the microbial population is high in the small intestine compared with stomach. The duodenum is mostly colonized by gram-positive bacilli and cocci, while enterococcus faecalis, lactobacilli, diphtheroid, and candida albicans inhabit the jejunum. The pH of the ileum is alkaline, supporting the growth of anaerobic gram-negative bacteria. Finally, the large intestine has the highest number of microbiota species in the human body. The main species of microbiota harboring in the large intestine are firmicutes, along with a small number of other microbes like bacteroides and proteobacteria.¹¹

Gut microbiota and nutrition. The nexus between the gut microbiota and nutrition is quite complex and an ongoing active area of scientific studies. The relationship seems to be cyclic, as it is known that gut microbiota plays a key role in human nutrition. Diversity and type of nutrients in the gut are regarded as significant factors that specify the growth and dominance of microbial species commensal.¹² Several studies have clarified that various types of diet, such as vegan, regular, organic, or maternal diets, influence gut microbiota.¹³ Reports also illustrate how gut microbiota help in digestion and assimilation of food by affecting gene expression in the small intestine. Several functional and metabolic activities are influenced by the gut's microbiota, especially the process of nourishing the body. The primary function of gut microbiota with respect to nutrition is the fermentation of carbohydrates, proteins, and synthesis of different vitamins, such as vitamin B12 and vitamin K. Furthermore, the human gut can digest most of the nutrients in the stomach and small intestine. However, the remaining nutrients, such as carbohydrates and proteins, which are not digested in the stomach or small intestine, will eventually move into the large intestine and be digested by the normal microbiota present. As a result, the normal microbiota present in the large intestine contributes significantly to digestion and extraction of calories, ranging from 10-30% of total ingested nutrients.¹⁴

Gut microbiota and carbohydrate fermentation. The human gut cannot digest the complex components of

Disclosure. Authors have no conflict of interests, and the work was not supported or funded by any drug company.

carbohydrates, such as polysaccharides. For instance, *Bacteroides thetaiotaomicron*, residing in the gut microbiota, has 226 glycoside hydrolases. Here, gut microbiota plays an essential role in the digestion of carbohydrates because the human genome encodes for 319 human glycoside hydrolases falling into 4 categories based on their similarity analyses.¹⁵ The microbiota residing in the distal gut tract can digest complex nutrient components, and anaerobic bacteria can ferment this component into a variety of products, such as short-chain fatty acids, acetate, and butyrate. These products can be absorbed easily through the colonocytes present in the wall of the colon. The short-chain fatty acids play an important function by providing mechanical strength to cells, maintaining cellular integrity.¹⁶

Interestingly, it has been found that short-chain fatty acids are important for the lungs, as they protect the host against inflammation of the lungs due to allergies. Furthermore, they also play a significant role in blood circulation and water absorption through the digestive tract. Short-chain fatty acids are a vital component of machinery for regulating the metabolism of food in the body. Furthermore, colonial epithelial cells require a sufficient amount of butyrate to carry out metabolic activity. It seems that the propionate might play a key role in the liver for gluconeogenesis or regulation of cholesterol synthesis.¹⁶ Acetate has been documented as the source of energy for peripheral tissues. It might play an important role in the synthesis of cholesterol and lipogenesis in the liver.¹⁷

Gut microbiota and obesity. An important benefit of gut microbiota in the human body is regulating energy absorption, providing biomolecules like proteins, carbohydrates, and fats. A variety of metabolic pathways fulfill caloric requirements and provide the necessary energy-providing molecule, mainly the adenosine triphosphate. Gut microbiota can affect the host's food metabolism in various ways, and it may also contribute to the regulation of energy.¹⁸ Recent reports also confirm that gut microbiota can decrease the expression of the fasting-induced adipocyte factor (FIAF), which reduces the level of lipoproteins leading to the deposition of fat in adipose tissue.¹⁹ Additionally, gut microbiota ferments undigested polysaccharides to produce monosaccharides and complex fats into short-chain fatty acids for easy absorption through the intestinal wall. The short-chain fatty acids bind to the G protein-coupled 41/43 receptors, which then trigger PYY peptide production. Production of Peptide YY (PYY) peptide inhibits the gut and gut microbiota's motility, which allows the gut microbiota to ferment

more polysaccharides.¹⁶ As a result, it appears that obesity is a consequence of gut microbiota activity acquiring and assimilating energy from undigested food, leading to the storage of extra calories as fat in the adipose tissue. Based on these observations, there is an obvious need to identify and classify the gut microbiota present in lean and obese people to understand the complexity of the association between gut microbiota and obesity. To address the above questions, a group of researchers found that gut microbiota communities are different in obese people than healthy people.

Further studies have demonstrated that the level of firmicutes is significantly higher in obese people, along with a 50% decrease in the number of bacteroides than lean people.²⁰ In the past, animal studies have confirmed such findings are corroborating with those in humans. Scientific studies have also demonstrated the relationship between gut microbiota and obesity in humans.²¹ The findings suggest that changes in the diet resulted in an increase of bacteroids and reduction of firmicutes.

Gut microbiota after bariatric surgery. The bariatric surgery, also known as Roux-en-Y gastric bypass and sleeve gastrectomy, strongly impacts gut microbiota. This is due to the reason that both procedures involve compartmentalizing the stomach and intestine. Numerous studies demonstrate the effects of this treatment strategy geared towards weight loss and controlling obesity had adverse influences on normal gut microflora.²² The alterations in gut microbiota after Roux-en-Y gastric bypass or sleeve gastrectomy contribute to reducing body weight.²³ This change in gut microbiota can have a negative effect on stable weight loss due to the increased abundance of Gammaproteobacteria.²⁴ Bariatric surgery benefits in weight loss have been ascertained. Its harmful impact on the gut microbiome plays a major role in supplying essential nutrients for various metabolic pathways. Comparing the 2 techniques used in bariatric surgery, the sleeve gastrectomy showed stability in the diversity of gut microbiota and caused less alteration of gut microbiota composition. Notably, the microbial species affected by weight loss procedures also differ.²⁵ The study also shows that sleeve gastrectomy decreases firmicute, whereas Roux-en-gastric increases bacteroides and proteobacteria. Differential changes could be due to procedural manipulations. After Roux-en-Y gastric bypass surgery, the alteration of gut microbiota can be attributed to many causes, including reducing acid secretion, allowing gram-positive bacteria to survive and grow. Another reason for the alteration of gut microbiota after Roux-en-Y gastric bypass surgery is an

increase in the level of oxygen in the gut, leading to a decrease in the number of obligate aerobes and allowing the growth of facultative anaerobes.

Further research work. The above studies provide an existing state of knowledge related to gut microbiota and obesity; however, many questions remain unanswered. In future altering gut microbiota could be one of the non-surgical therapeutic methods for weight reduction. For example, several studies are alluding to the possibility of weight reduction by altering gut microbiota through demonstrating the impact of antibiotics on gut microbiota.²⁶ The potential of probiotics specific toward reducing fat absorption from the gut is another unique methodology awaiting further translational application.²⁷ Gut control all the absorption of nutrients and blocking fatty material access toward metabolic cascade through harnessing microbes or through alternative methodologies are the future consideration towards maintaining healthy weight among humans. This is an active area of investigation, and technological advancements will help overcome obesity rather than utilize surgical procedures like bariatric surgery and others.²⁸

In conclusion, the purpose of this review is to compile existing knowledge on normal gut microbiota and how it affects the human nutritional cycle (**Figure 1**). Gut microbiota comprises the variety of microbes existing in the human alimentary canal. Thus, investigating gut microbiota and its interactions with different aspects of the nutritional cycle such as nutrition, human metabolism, and pathogenesis of obesity is of utmost importance. Several studies have shown that diet may

impact the composition of gut microbiota. Additionally, gut microbiota contributes to digesting carbohydrates that the gut cannot otherwise digest. Thus, it provides the gut with fermented carbohydrate products, which can be absorbed by epithelial cells, meaning many calories are produced from the fermented component in the body. This contribution of gut microbiota towards generation of extra calories results in the storage of excess calories as fat, ultimately linked with obesity. The composition of gut microbiota differs in obese people in comparison with lean people.

Moreover, bariatric surgeries such as Roux-en-Y gastric bypass and sleeve gastrectomy influence the composition of gut microbiota. Researchers have noted changes in gut microbiota composition after Roux-en-Y gastric bypass, but it appears that sleeve gastrectomy differentially changes gut microbiota composition. The increased number of gammaproteobacteria after Roux-en-Y gastric bypass may be responsible for the stability of body weight. A modest number of studies have examined the impact of different methods for reducing obesity, such as modifying gut microbiota and several others. A careful review of the existing literature suggests that soon, prebiotics and probiotics may contribute to a great extent in the treatment of obesity since these can have a considerable effect on gut microbiota composition.

Acknowledgment. The authors gratefully acknowledge Cambridge Proofreading LLC for English language editing.

References

1. Bonder MJ, Kurilshikov A, Tigchelaar EF, Mujagic Z, Imhann F, Vila AV, et al. The effect of host genetics on the gut microbiome. *Nat Genet* 2016; 48: 1407-1412.
2. Li WZ, Stirling K, Yang JJ, Zhang L. Gut microbiota and diabetes: from correlation to causality and mechanism. *World J Diabetes* 2020; 11: 293-308.
3. Lazar V, Ditu LM, Pircalabioru GG, Gheorghe I, Curutiu C, Holban AM, et al. Aspects of gut microbiota and immune system interactions in infectious diseases, immunopathology, and cancer. *Front Immunol* 2018; 9: 1830.
4. Rowland I, Gibson G, Heinken A, Scott K, Swann J, Thiele I, et al. Gut microbiota functions: metabolism of nutrients and other food components. *Eur J Nutr* 2018; 57: 1-24.
5. Khan MJ, Gerasimidis K, Edwards CA, Shaikh MG. Role of gut microbiota in the aetiology of obesity: proposed mechanisms and review of the literature. *J Obes* 2016; 2016: 7353642.
6. Hosaka H, Kawamura M, Hirano T, Hakamata W, Nishio T. Utilization of sucrose and analog disaccharides by human intestinal bifidobacteria and lactobacilli: search of the bifidobacteria enzymes involved in the degradation of these disaccharides. *Microbiol Res* 2020; 240: 126558.

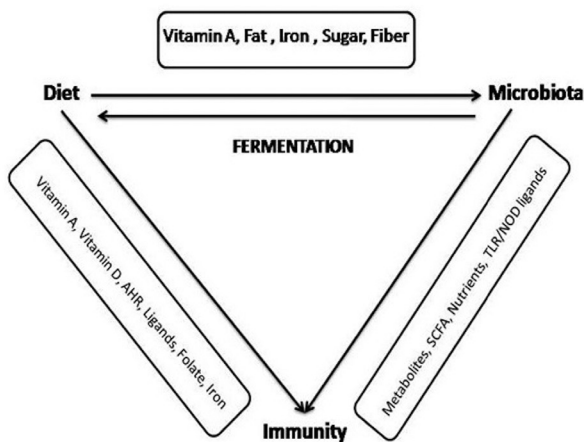


Figure 1 - The interdependence of diet, microbiota, and immune responses.

7. Laursen ME, Bahl MI, Michaelsen KF, Licht TR. First foods and gut microbes. *Front Microbiol* 2017; 8: 356.
8. Shao Y, Forster SC, Tsaliki E, Vervier K, Strang A, Simpson N, et al. Stunted microbiota and opportunistic pathogen colonization in caesarean-section birth. *Nature* 2019; 574: 117-121.
9. van den Elsen LWJ, Garssen J, Burcelin R, Verhasselt V. Shaping the gut microbiota by breastfeeding: the gateway to allergy prevention? *Front Pediatr* 2019; 7: 47.
10. Kaur K, Khatri I, Akhtar A, Subramanian S, Ramya TNC. Metagenomics analysis reveals features unique to Indian distal gut microbiota. *PLoS One* 2020; 15: e0231197.
11. Yuan C, Graham M, Staley C, Subramanian S. Mucosal microbiota and metabolome along the intestinal tract reveal a location-specific relationship. *mSystems* 2020; 5: e00055-e00020.
12. Levy R, Magis AT, Earls JC, Manor O, Wilmanski T, Lovejoy J, et al. Longitudinal analysis reveals transition barriers between dominant ecological states in the gut microbiome. *Proc Natl Acad Sci U S A* 2020; 117: 13839-13845.
13. Leeming ER, Johnson AJ, Spector TD, Le Roy CI. Effect of diet on the gut microbiota: rethinking intervention duration. *Nutrients* 2019; 11: 2862.
14. Azzouz LL, Sharma S. Physiology, large intestine. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2020.
15. Nakamura T, Fahmi M, Tanaka J, Seki K, Kubota Y, Ito M. Genome-wide analysis of whole human glycoside hydrolases by data-driven analysis in Silico. *Int J Mol Sci* 2019; 20: 6290.
16. Silva YP, Bernardi A, Frozza RL. The role of short-chain fatty acids from gut microbiota in gut-brain communication. *Front Endocrinol (Lausanne)* 2020; 11: 25.
17. Barton W, O'Sullivan O, Cotter PD. Metabolic phenotyping of the human microbiome. *F1000Res* 2019; 8: F1000 Faculty Rev-1956.
18. Inami A, Kiyono H, Kurashima Y. ATP as a pathophysiologic mediator of bacteria-host crosstalk in the gastrointestinal tract. *Int J Mol Sci* 2018; 19: 2371.
19. Amabebe E, Robert FO, Agbalalah T, Orubu ESF. Microbial dysbiosis-induced obesity: role of gut microbiota in homeostasis of energy metabolism. *Br J Nutr* 2020; 123: 1127-1137.
20. Magne F, Gotteland M, Gauthier L, Zazueta A, Pesoa S, Navarrete P, et al. The firmicutes/bacteroidetes ratio: a relevant marker of gut dysbiosis in obese patients? *Nutrients* 2020; 12: 1474.
21. Ahmad A, Yang W, Chen G, Shafiq M, Javed S, Ali Zaidi SS, et al. Analysis of gut microbiota of obese individuals with type 2 diabetes and healthy individuals. *PLoS One* 2019; 14: e0226372.
22. Cook J, Lehne C, Weiland A, Archid R, Ritze Y, Bauer K, et al. Gut microbiota, probiotics and psychological states and behaviors after bariatric surgery-a systematic review of their interrelation. *Nutrients* 2020; 12: 2396.
23. O'Brien PE, Hindle A, Brennan L, Skinner S, Burton P, Smith A, et al. Long-term outcomes after bariatric surgery: a systematic review and meta-analysis of weight loss at 10 or more years for all bariatric procedures and a single-centre review of 20-year outcomes after adjustable gastric banding. *Obes Surg* 2019; 29: 3-14.
24. Debédat J, Clément K, Aron-Wisniewsky J. Gut microbiota dysbiosis in human obesity: impact of bariatric surgery. *Curr Obes Rep* 2019; 8: 229-242.
25. Davies NK, O'Sullivan JM, Plank LD, Murphy R. Altered gut microbiome after bariatric surgery and its association with metabolic benefits: a systematic review. *Surg Obes Relat Dis* 2019; 15: 656-665.
26. Li Y, Liu Q, Peng C, Ruan B. Both gut microbiota and differentially expressed proteins are relevant to the development of obesity. *Biomed Res Int* 2020; 2020: 5376108.
27. Mazloom K, Siddiqi I, Covasa M. Probiotics: how effective are they in the fight against obesity? *Nutrients* 2019; 11: 258.
28. Berry EM. The obesity pandemic-whose responsibility? No blame, no shame, not more of the same. *Front Nutr* 2020; 7: 2.