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The Role of Microbiota on the Incidence of Obesity

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Abstract

Obesity is predicted to become a global public health problem, especially in developing countries. Obesity is characterized by a body mass index (BMI) of 30 or more, which is calculated by dividing a person's weight by the square of their height (in kilograms per square meter). The incidence of obesity by age increased from 4.6% in 1980 to 14.0% in 2019. According to the World Health Organization (WHO), around 2 billion adults are classified as overweight, while another 650 million people are categorized as obese. Based on a national survey, the obesity rate in Indonesia is 23.1%, while in South Sulawesi province it is 31.6% (Riskesdas, 2018). This can alter the gut microbiota structurally and functionally, and the gut microbiota can also modulate nutritional status. A certain abundance and diversity of bacteria may facilitate energy storage and metabolic pathways that lead to obesity. Dietary interventions with probiotics, prebiotics, or synbiotics may be effective in counteracting the disturbances observed in the gut microbiota during obesity or unbalanced diets, as they may be able to reduce and maintain body weight. Intestinal anaerobic bacteria, including Firmicute and bacteroids, can hydrolyze carbohydrates that cannot be digested by the intestine, obtaining short chain fatty acids (SCFA) including acetate, propionate and butyrate, which have an impact on human health. Therefore, anaerobic bacteria can inhibit obesity.

Introduction

Obesity and other related disorders have reached alarming stages around the world. Obesity is a chronic and recurrent condition resulting from excessive or improper accumulation of fat. The last few decades have seen an exponential increase in the number of people suffering from obesity. A sedentary lifestyle and increased food consumption are considered to be the main causes of this obesity epidemic. Environmental and genetic factors are also involved, including changes in gut microbiota that play a role in the development of metabolic disorders. Obesity has serious health impacts, including an increased risk of death, type 2 diabetes, and cardiovascular. This etiology is multifactorial, contributing factors include genetics, a high-fat diet (HFD), and gut microbiota. The gut microbiota, which consists mostly of anaerobic bacteria, facultative anaerobic bacteria, and aerobic bacteria, is a dynamic ecosystem that coexists with its host. The gut microbiota plays an important role in maintaining host health through vitamin production, nutrient absorption, and secretion of small molecules involved in immune regulation, angiogenesis, and nerve function (Baothman et al., 2016; Fan et al., 2023).

The gut microbiota relies on foods that digestion cannot, mucus that is from the gut, and dead cells that are secreted as nutrients to maintain high population levels. An active gut microbiota will produce a large number of physiologically active substances, including short-chain fatty acids, vitamins, and health-beneficial products such as anti-inflammatory, analgesic, and antioxidant products, as well as potentially harmful products such as neurotoxins, carcinogens. , and immunotoxins. These products can enter the blood, directly regulate gene expression, and affect human immune and metabolic processes. Therefore, a healthy gut microbiota is essential for maintaining the body's metabolism and energy balance. An imbalance of gut microbiota can lead to metabolic disorders and increase central appetite leading to obesity (Liu et al., 2021).

Methods

This study is a type of qualitative study using the article review method. As a qualitative study, this study uses a lot of literature from various journals, both journals in the national scope such as the Journal of Health Research Implementation Media, Riskendas reports and so on. While international journals are also used as a complement as well as adding to scientific discussions related to microbiota and obesity which are the focus of study in this study. The data obtained were then processed in the form of a systematic study as an effort to answer the main question of research, namely the role of microbiota on the incidence of obesity.

In addition, there are two important concepts that need to be explained in this study, namely obesity and microbiota, namely as follows.

Obesity

Obesity is projected to become a serious problem in developing countries. The World Health Organization (WHO) Obesity Expert Consultation has warned about the increasing prevalence of obesity in developing countries. An earlier WHO report on Diet, Nutrition and Prevention of Chronic Diseases cited obesity as a major risk factor for all noncommunicable diseases. Obesity is characterized by a body mass index (BMI) equal to or greater than 30, which is calculated by dividing a person's weight by the square of his height. In contrast, overweight was described as having a BMI ranging from 25.0 to 29.9. Being overweight or obese is associated with a higher number of deaths compared to being underweight, and it is a more common problem worldwide than being underweight. Body Mass Index (BMI) is determined by dividing a person's weight in kilograms by the square of his height in meters. To estimate BMI using pounds and inches, use: [weight (pounds)/height (inches) 2]. World Health Organization (WHO) Classification of Adult Body Mass Index in Table 1 (Harbuwono et al., 2018; Chaithanya et al., 2020; Lin & Li, 2021).

Table 1. World Health Organization (WHO) Adult Body Mass Index Classification

Overweight and Obesity Classification	BMI (kg/m2)
Underweight	< 18.5
Usual	18.5 – 24.9
Obesity	25.0 – 29.9
Obesity Class 1	30.0 – 34.9
Obesity Class 2	35.0 – 39.0
Obesity Class 3	> 40

The incidence of obesity across different age groups increased from 4.6% in 1980 to 14.0% in 2019. Half of this increase occurred in the 22 years between 1980 and 2002 and the other half occurred in the 17 years between 2002 and 2019. Women's dominance is constant in the prevalence rate of obesity compared to men. According to WHO, there are 2 billion people with obesity, while 650 million people are obese. If this figure does not slow, an estimated 2.7 billion adults will be obese and 1 billion people will be obese by 2025. The prevalence of obesity increased sharply between 1980 and 2019 from 3.2% to 12.2% in men, and from 6% to 15.7% in women. The fact that women are constantly leading in terms of the proportion of

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obesity is to be suspected of a higher body fat percentage in biologically driven women. Riskesdas' findings showed that the incidence of overnutrition/obesity in adolescents aged 16-18 years increased from 7.3% in 2013 to 13.5% in 2018. Based on the national survey, the obesity rate in Indonesia is 23.1%, lower than the central obesity rate of 28%. The percentage of men and women who were obese was 16.9% and 28.6%. While the prevalence by province in South Sulawesi is 31.6% (Boutari, 2020; Harbuwono et al., 2018; Masud & Sahariah Rowa, 2023).

Risk factors for obesity in individuals between the ages of 25 and 65 include sex, smoking behavior, fat consumption, and the interaction between smoking habits and smoking duration. The variable that exerts a great influence on obesity is gender . Genetic factors There are three types of genetic obesity: monogenic, polygenic and syndromic (Sudikno et al., 2018) (Masood & Moorthy, 2023). *First*, monogenous obesity occurs as a result of mutations or deficiencies of one gene and is a rare but severe cause of obesity. *Secondly*, polygenic obesity, caused by the presence of several gene variants simultaneously, has an accumulative effect. *Third*, syndromic obesity, associated with signs of other developmental disorders, and may or may not be accompanied by congenital abnormalities. syndrome; Its characteristic sign is dysmorphic features and organ abnormalities.

Modifiable factors are as follows (Masood & Moorthy, 2023): (1) Epigenetics, alterations that affect genetic expression without altering the DNA sequence, it is obtained through interaction with the environment this risk can be reduced by healthy food choices, increased physical activity. (2) Physical inactivity, the association between physical activity and genetic risk scores for obesity were analyzed and showed that physical activity lowered the risk of obesity. In fact, those with higher genetic risk scores benefited the most despite moderate exercise. (3) Historically, the main dogma of obesity science was that obesity was simply a disorder of energy balance: calories in, calories out. If this energy-based obesity (EBM) model, is true, then basically exercising more and eating less should work for everyone. (4) Intrauterine environment, obesity in the mother has long been known as the strongest risk factor for childhood obesity Therefore, a stronger association between maternal and child fat mass suggests a possible role for the intrauterine environment in the development of obesity later in life. (5) Postnatal influences, the postnatal environment is equally important in determining the rate of weight gain throughout life. Postnatal factors that can be modified and affect weight later in life include: Sleep duration, duration of breastfeeding, and rate of weight gain in the baby. (6) Sleep is not enough, sleep regulates glucose metabolism and neuroendocrine function. Sleep deprivation reduces glucose intolerance, insulin sensitivity and leptin levels as well as increases cortisol and ghrelin levels (and hence appetite). (7) Drugs, certain therapeutic drugs cause significant weight gain in some people. (8) Medical conditions, cause weight gain through different mechanisms. (9) Socioeconomic status, the prevalence of severe obesity in children of acceptance age is almost three times higher in the poorest regions (i.e. 4.6% compared to only 1.3% in children living in the poorest areas). (10) Psychosocial stress: Stress increases chronic exposure to glucocorticoids (increases abdominal obesity) and contributes to the emotion/comfort of eating. (11) Environmental chemicals that interfere with the work of hormones in the human body are called endocrine disrupting chemicals (EDCs). EDC has a lipophilic structure so that it can interfere with hormonal work and disrupt normal endocrine function. (12) Gastrointestinal microbiomes, Gastrointestinal microbes called 'friends with benefits' consist of Firmicute, Bacteroids, Proteus, Actinomycetes and Fusobacteria. Two phyla are mostly seen inhabiting obese people: Firmicutes and Bacteroides. (13) The management of obesity is directly influenced by the approach of health professionals towards obesity and therefore, it is very important to evaluate our approach towards patients suffering from obesity.

The consequences of obesity on individuals and society are evident when considering the prevalence of obesity-related chronic diseases such as type 2 diabetes mellitus (T2D), hypertension, dyslipidemia, osteoarthritis, sleep apnea, and various forms of cancer. These conditions, coupled with associated disabilities, can significantly decrease productivity levels. There are many mechanisms underlying obesity complications. We'll look at two more prominent players; inflammation and the gut microbiome (Masood & Moorthy, 2023; Kinlen et al., 2018).

Inflammation

Obesity is associated with mild and persistent inflammation in the body, which is controlled by metabolic cells in reaction to overeating. This inflammatory state occurs in organs such as the liver, brain, pancreas, and adipose tissue and is involved in immunometabolic diseases

Gut microbiome

More and more attention is being paid to the role of the microbiome in the development of obesity-related complications. Gut microbes impact the body's metabolism through signaling pathways, which impact inflammation, fat accumulation, and insulin resistance. It has been proven that obesity is associated with major microbial changes.

Diabetes

The risk of T2DM increases with weight gain; A study of more than 21,000 adults within NHANES found the risk increased from 8% with normal weight to 43% in individuals with morbid obesity

Cardiovascular diseases

Hypertension: Children who are obese are approximately three times more likely to suffer from hypertension than children who are not obese. In adults, there is an almost linear relationship between BMI and BP and weight loss reduces blood pressure in most people with hypertension.

Dyslipidemia: The effects of obesity on lipid metabolism include high low-density lipoprotein cholesterol, very low-density lipoprotein cholesterol, triglycerides as well as low protective high-density lipoprotein cholesterol.

Coronary heart disease: Data from the NHANES study including mortality information of 2.3 million American adults suggest that obesity is associated with a significant increase in mortality from both CHD and other forms of CVD.

Heart failure: Obesity has been shown to affect the heart since childhood, with children who are obese having a much higher left ventricular mass.

Stroke: People who are obese are shown to be twice as likely to have a stroke, both ischemic and hemorrhagic

Neurological diseases

Vascular risk factors such as hypertension, dyslipidemia, and diabetes are all associated with an increased risk of dementia and Alzheimer's disease

Cancer

It is estimated that obesity accounts for -20% of all cancer cases In addition, the prognosis is worse in individuals with obesity who develop some type of cancer. A study found that obese women who had breast cancer were 46% more likely to develop distant metastases and 38% more likely to die than thin women.

Respiratory

Obstructive sleep apnea: Obesity has long been known to be a major pathogenic factor of OSA in adults. Obstructive sleep apnea (OSA) adversely affects many systems and is associated with hypertension, insulin resistance, liver dysfunction, systemic inflammation, and dyslipidemia.

Asthma: It is known that obesity increases the risk of asthma but the mechanisms underlying this are not yet fully understood. Inflammation causes, mechanical, immunological, hormonal and genetic have all been suspected

Immune system

Obesity causes dysregulation of the immune system that can be seen from minor with increased susceptibility to various types of infections, including infections at the surgical site, urinary tract, nosocomial and skin.

Gastrointestinal tract

Obesity is associated with a greater risk of pancreatitis and is a poor prognostic factor in the disease. It is also considered to be the main reason for the 2-fold increase in the incidence of gastroesophageal reflux disease and its associated conditions.

Kidney disease

Obesity is associated with a greater risk of kidney stones and urinary incontinence in women, while obesity-related glomerulopathy has an increased prevalence along with obesity.

Fertility

In men, obesity is associated with reduced sperm count and increased rates of erectile dysfunction. In women, it also leads to reduced fertility, poorer fertility treatment outcomes, and more miscarriages

Mesculoskeletal

Obesity is associated with a significant decrease in physical activity levels and is one of the main risk factors for osteoarthritis.

Psychosocial

Depression is prevalent in obese people, especially in women and young people, while weight loss is associated with improved mood.

Microbiota

The human gut microbiota is an ecological entity that includes bacteria, yeasts, viruses, and parasites, resulting in a total of about 100 trillion microorganisms. The composition of healthy gut microbiota is dominated by up to 90% of phylum *Firmicute* and *bacteroids*. The phylum of *Firmicute* includes several genera, the most common (up to 95%) being *Lactobacillus, Bacillus, Enterococcus, Ruminicoccus and Klostridium*. The gut microbiota is one of the main components of the gut ecosystem, and plays an important role for human health, including a shielding effect with intestinal barrier protection, the formation and maturation of the immune system, regulation of human metabolism and nutrition, and drug absorption (Rinninella et al., 2023).

The definition of a healthy microbiota represents the alpha diversity of gut microbiota, an ecological concept that refers to the number and distribution of different species, appears to be a reliable marker of microbiome health. The gut microbiota is a dynamic ecosystem of several aspects, namely lifestyle, and especially diet. Since eating habits tend to differ according to geographical factors, this variability is also seen to be reflected in the microbiota of different populations. In general, subjects with obesity and overweight tend to show a lower diversity of the gut microbiome (Rinninella et al., 2023).

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The diverse human microbiome has important metabolic activities that are essential for the proper functioning of mammalian enzymes, in the intestinal mucosa and liver and host metabolism. Gut microbiota affects the health of the body by shaping the biochemical profile of food. The important role of gut microbiota in human immunity has prompted research to investigate the contribution of certain microbes in metabolic pathways, particularly in the metabolism of food components (Afzaal et al., 2022).

Microbiota ferments undigested complex carbohydrates, also known as microbiota-accessible carbohydrates (MAC), causing increased levels of SCFA and, as a result, providing positive health effects. Unsaturated vegetable fats in the diet reduce harmful bacteria while increasing the number of Bifido bacterium and butyrate-producing bacteria (Roseburia and Faekali bacterium), all of which have been linked to positive health effects (Afzaal et al., 2022).

Current advances show that the human microbiota is closely involved in nutrient extraction, metabolism, and immunity. Microbiota can influence biological processes through several mechanisms. For the extraction of energy and nutrients from food, the microbiota plays an important role due to its versatile metabolic genes that provide unique enzymes and independent biochemical pathways. In addition, the biosynthesis of bioactive molecules such as vitamins, amino acids, and lipids is also highly dependent on the gut microbiota. Nutrition regulates the composition and function of gut microbiota by influencing microbial diversity, intestinal barrier permeability, immune function, energy collection, macromolecule metabolism, and enzyme activity. The importance of adequate and balanced nutrition with respect to the energy and macronutrient components for the gut microbiota (Hou et al., 2022; İlhan, 2018).

Result and Discussion

Obesity can alter the gut microbiota structurally and functionally, and the gut microbiota can also modulate nutritional status. The abundant and diverse number of certain bacteria can facilitate energy storage and metabolic pathways that lead to obesity. This suggests that altering the gut microbiota by food or other means may exert beneficial effects by restoring the functional integrity of the gut and reversing the dysbiosis that characterizes obesity. The gut microbiota of obese subjects was found to be higher in Firmicute and lower bacterioid ratio compared to underweight subjects, but after 1 year of diet therapy, an inverted profile was found (Zsálig et al., 2023).

The composition of gut microbiota also varies depending on the severity of obesity. With obesity, the genera *Bacteroidales*, such as *aLactobacillus spp., Bifidobacterium spp., Bacteroids spp., and Enterococcus spp.,* as well as *Firmicute* and *bacteroids* and *Enterobakteriaceae* species increased, while the proportion of *Clostridia*, including *Klostridium leptum* and *Enterobakter spp*. Decreased. In particular, significant reductions in the composition of the bacterial genera *Akkermansia, Faekalibakterium, Oscillibakter* and *Alistipe* have been shown in obese people. Higher levels of *Lactobacillus reuteri* and lower levels of *Methanobrevibacter smithii* were associated with obesity leading to significant weight gain, while *Bifidobacterium* animalis and *Methanobrevibacter smithii* and other Lactobacillus species were found in higher numbers in normal-weight individuals. The exact mechanism of action of bacteria in human models is unclear, but potentially effective in reducing body weight including through the production of SCFAs (acetic acid, butyric acid) and through strong inhibition of de novo lipogenesis. in the regulation of liver lipid metabolism (Zsálig et al., 2023).

In fact, eating high-calorie foods and replacing leisure physical activity with sedentary activity are major risk factors for obesity and obesity-related diseases, ultimately resulting in excess energy stored in the body. Excess lipid consumption from a high-calorie diet results in lipid buildup in subcutaneous and visceral adipose tissue, which can cause adipose tissue to be unable to store excess energy as triglycerides, causing excess lipids to enter the systemic circulation. Excessive systemic circulation and absorption of lipids into non-adipose tissues, which cannot easily undergo fatty acid oxidation (FAO) to increase the availability of fatty acids, causing ectopic fat storage, Diet is a major factor influencing the imbalance of gut microbiota (Al-Assal et al., 2018).

Dietary interventions with probiotics, prebiotics, or synbiotics may be effective in reversing disturbances observed in the gut microbiota during obesity or an unbalanced diet, as such interventions may be able to reduce and maintain body weight. In randomized controlled clinical trials, symbiosis is given to individuals participating in a weight loss program. The probiotics used are *Lactobacillus acidophilus, Bifidobacterium lactis, Bifidobacterium longum,* and *Bifidobacterium bifidum* and the prebiotic components are a mixture of galacto oligosaccharides (Zsálig et al., 2023).

A variety of factors including food choices, behavior, heredity and gut microbiota can contribute to obesity. Food choices directly affect calorie intake, and daily consumption of sugary drinks increases the risk of obesity. There is evidence that microbiota variation plays a greater role in the pathogenesis of obesity. The gut microbiota in obese and thin people is different, and the microbiota in obese people has an increased ability to get energy from their food. Colonization of the 'obese microbiota' in sterile mice resulted in a significant increase in fat compared to colonization of the 'lean microbiota'. Intestinal anaerobic bacteria, including *Firmicute* and *bacteroids* , can hydrolyze carbohydrates that cannot be digested by the intestine, obtained by SCFAs including acetate, propionate and butyrate, which have an impact on human health. The free fatty acid receptor 3/G-protein coupled receptor 41 (FFAR3/GPR41) is an SCFA receptor, associated with reduced food intake, increased energy consumption, and leptin hormone expression. Therefore, anaerobic bacteria can inhibit obesity (Duan et al., 2021).

It is known that supplementation with products containing live microorganisms, known as probiotics, improves the barrier function of the intestinal epithelium and increases the production of mucus thereby reducing some digestive problems such as diarrhea, abdominal pain, lactose intolerance, etc. Interestingly, probiotic supplementation has emerged as a weight loss effort. strategies based on presumed anorexigenic effects by increasing the production of SCFAs, which play a role in oxidation fatty acids as well as intestinal hormone secretion (peptide YY and glucagon- and leptin-like peptides in adipocytes. The potential effects of probiotic supplementation on weight loss can be enhanced when combined with prebiotics, which are certain groups of indigestible and fermented foods that provide more stomach volume during meals and are substrates for microorganisms in the intestinal lumen. So, the combination of probiotics and prebiotics, called synbiotics, deserves attention for their potential in improving obesity indicators. Species of *Lactobacillus* and *Bifidobacterium* genera are components of probiotic supplements in the area of weight loss; however, optimal dosing regimens and sensible clinical effects are far from clear. In addition to obesity, similar modest effects also occur in patients suffering from obesity and its metabolic-related diseases. Not only probiotics but also supplementation with symbiosis showed little clinical impact in improving anthropometric indicators of obesity (Tassoni et al., 2023).

Conclusion

Obesity has become a socioeconomic and health problem in the world due to its global prevalence and increasing incidence rates, so it is urgent to seek more effective therapeutic interventions. The important role of gut microbiota in major metabolic diseases impacting major pathways such as energy homeostasis and inflammation. Lifestyle changes involving increased food consumption and reduced exercise and gut microbiota contribute to greater metabolic disease. As a result, a better understanding and utilization of various prebiotic bacteria and probiotics may prove beneficial in the treatment of metabolic diseases in the

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future. Numerous pieces of evidence have found that gut microbiota, as an environmental factor, has been an important contributor to the etiology of obesity. Overall the microbiota diversity and composition of gut has changed significantly compared to obesity controls. Overall, the microbiota of obese subjects showed low diversity, higher abundance of *Firmicutes*, and increased *Firmicutes/Bacteroidetes ratio*.

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