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Gender Inequality in Obesity: the Role of Intestinal Flora

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Abstract: The prevalence of obesity has become a serious problem spreading around the world. With the prosperity of the food processing industry, people now have access to a wide variety of foods. Because of the lack of awareness of health, many individuals are at risk of an imbalance between caloric intake and expenditure, leading to widespread obesity. Not only is obesity on the rise but there has also been no significant national success in combating it over the past 44 years. This research will focus on the gender difference in the obesity rate which aims to provide reliable data for the obesity prevention strategies. The paper offers insights into the nature of obesity and how multiple factors contribute to obesity. The primary causes are categorized into three pathways: neural, dietary, and compositional, with the neural pathway being the most dominant. This research is based on global and regional statistics from various regions, including America, Turkey, Europe, and Asia. The general conclusion shows that females are more prone to obesity than males. However, there are some deficiencies in the conclusion due to the complexity of factors such as genetics, dietary habits, and primary physical activities.

Keywords: obesity, gender inequality, gut microbiota, gut-microbiota-brain axis

1. Introduction

Obesity is a physical condition caused by excess fat accumulation due to a long-term imbalance between caloric intake and expenditure. Sometimes, it can be considered as a neural disorder. Obesity is usually measured by BMI (Body Mass Index), with its classification listed as follows [1].

Severely underweight - BMI less than 16.5kg/m^2
Underweight - BMI under 18.5 kg/m^2
Normal weight - BMI greater than or equal to 18.5 to 24.9 kg/m^2
Overweigh - BMI greater than or equal to 25 to 29.9 kg/m^2
Obesity - BMI greater than or equal to 30 kg/m^2
* Obesity class I - BMI 30 to 34.9 kg/m^2
* Obesity class II - BMI 35 to 39.9 kg/m^2
* Obesity class III - BMI greater than or equal to 40 kg/m^2 (also referred to as severe, extreme, or massive obesity)

For the Asian and South Asian populations:
* Overweight - BMI between 23 and 24.9 kg/m^2
* Obesity - BMI greater than 25 kg/m^2

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Obesity can be classified into the genetic-caused obesity and the diet-caused obesity. In fact, 80% of the human population own genes that may cause obesity, which represents a high hereditary rate of the genes [1]. Genetic obesity can result in childhood obesity and become much more influential as children experience their mid-childhood period [2]. On the other hand, obesity has also shown relevance to the surrounding environment. People who consume more fat, carbohydrates, and other energy-dense foods tend to experience a caloric imbalance, which increases the likelihood of obesity. Besides, obesity is often accompanied by various complications, such as diabetes, cardiovascular disease, heart disease, and hypertension.

The intestinal flora, the other important concept of this paper, refers to microbes that exist in the human gut. The most common intestinal microbes include *Bacteroides*, and *Firmicute* [3]. These microbiota help digest food and stimulate or inhibit food intake, while an imbalance in intestinal flora may increase the risk of obesity, cardiovascular diseases, and malnutrition.

Many countries have made efforts to control the obesity rate. Although the normal suggestions need people's self-discipline and may be ineffective for some particular individuals, launching compulsive strategies, such as making obesity illegal, is a violation of human rights and therefore impractical. More specialized methods should be developed for obese people with different physical conditions. This paper aims to research the gender differences in obesity rate caused by intestinal flora, which can provide scientific evidence for health regulation plans for different genders.

2. The Impact of Intestinal Flora on Obesity

In this part, various aspects contributing to obesity will be elaborated, with a particular focus on the gut microbiota, specifically the gut-microbiota-brain axis.

2.1. Gut-microbiota-brain Axis

The Gut-microbiota-brain axis gets its name from its bidirectional effect. The gut and brain are connected in multiple ways including the neuroendocrine system, immune system, enteric nervous system, and vagus system. For neural pathways, there are 2 main connections: the automatic nervous system and the vagus nerve. Vagus nerve (VN) is a kind of nervous fibers that physically link the brain and gut together, playing a crucial role in the autonomic nervous system (ANS). It serves as a major passway of the signals sent by receptors to the central nervous system (CNS). To be more specific, chemoreceptors in the human gut detect changes in the gut microbiota composition, leading to alterations in the metabolites they release. This variation leads to calcium signaling secretion that may be transmitted to specific fibers of the vagus nerve in the gut epithelium. At the same time, as said above, the vagus nerves can relay signals from the CNS to visceral organs or tissues. In conclusion, its main functions include transporting bidirectional signals between the brain and the gut [4]. Its function determines its key role in human weight homeostasis. If the vagus nerve is interrupted, significant changes in gut microbiota composition may fail to stimulate the secretion of specific signaling molecules to the brain, potentially resulting in neural disorders that contribute to overeating or an increase in adipose tissue. Hormones like glucagon-like peptide 1 (GLP-1), peptide YY(PYY), ghrelin are all responsible for regulating human food-intake behavior. Some gut bacteria can modify the secretion of gut hormone, including GLP-1, ghrelin, PYY, and LEP, thus affecting the hypothalamic neuroendocrine pathways related to appetite and satiety. To be more specific, the gut microbiota produces SCFA which can bind to the receptors on the enteroendocrine cells (EECs) and stimulate the secretion of enteric hormone. On the other hand, the SCFA like acetate will suppress appetite through central hypothalamic mechanisms. Also, the activation of the taste receptors in (EECs) will result in the ghrelin, GLP-1, and cholecystokinin secretion.

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2.2. Absorption of Fat and Liquid in Guts

It is introduced above that the fundamental cause of obesity is too much intake of calories. The calories are mainly gained from carbohydrates, lipids, and fat. However, the calories produced by carbohydrates are significantly different from those produced by fats or lipids, which means, in other words, the calories produced by lipids or fats tend to cause obesity. Firstly, the fat consumed has an inverse correlation with the amount of fat oxidized [5]. The less the fat is oxidized, the more fat is stored in the body as white adipose tissue. What's more, research on high-fat diet (HFD) effects in rodents suggests that HFD promotes steatosis, changes in β-oxidation, generation and consequences of oxidants, which will finally result in a gain in body weight of rodents. Apart from that, excessive nutrient intake driven by HFD leads to two consequences—physical inactivity and overnutrition—that can overwhelm the adipose tissue's ability to manage energy, and meanwhile, this overload stimulates the efflux of non-esterified fatty acids and contributes to the release of proinflammatory cytokines and adipokines, which may result in ectopic fat deposition in the liver, muscle, and heart [6]. This deposition in the organs can bring a higher risk of getting obesity and its correlated metabolic diseases like cardiovascular diseases, coronary heart disease, and inflammation. Furthermore, lipid intake negatively impacts metabolism. In the same experiment of rodents, the researchers have also found that different types of lipid intake elicit varying metabolic responses. For example, diets rich in saturated fatty acids lead to decreased basal metabolic rates, higher body weights and fat gain when compared to diets containing predominantly unsaturated fatty acids [7]. Apart from that, the consumption of saturated fatty acids relates to the development of the resistance of insulin, which projects a metabolic disability in blood glucose regulation. By contrast, the intake of unsaturated fatty acids may post a protective mechanism or even improve insulin sensitivity [8].

What's more, the differences in resistance to loss of energy can result from a sex dimorphism of the hypothalamic melanocortin system. In the experiment of rodents, male mice show a decreased density of anorexigenic neuropeptide pro-opiomelanocortin (POMC) neuronal fibers in the hypothalamic arcuate nucleus, and decreased POMC gene and protein expression, which relate to an increased energy intake. However, male rats are more sensitive to the anorectic action of insulin injected into the brain, which can help them regulate their glucose level and avoid overaccumulation of adipose tissue [9]. Accordingly, compared with male mice, excessive intake places a greater burden on female mice's digestive systems.

2.3. Statistical Differences in Specific Microbiota Associated with Obesity

Intestinal flora can affect body weight in many ways, including energy absorption, metabolic processes, hormone secretion, and fat storage. The intestinal flora in human guts is extreme abundant, which means that there will be complex effects caused by specific microbiota and interaction between them. And also, the composition of human gut microbiota varies from person to person due to factors such as genetics, diet, and population differences. In a healthy gut environment, gut microbiota consists of *Firmicutes, Bacteroides, Proteus, Actinomycetes, Fusobacteria*, and *Verrucomicrobia*, among which *Firmicutes* and *Bacteroides* dominate [10]. A lower *Firmicutes/Bacteroidetes* (F/B) ratio correlates with health, for example, mice have a significantly lower F/B ratio compared to their obese counterparts. This trend is observed not only in mice but also in humans. A statistical survey in Ukraine proved that the *Firmicutes/Bacteroides* ratio shows a positive relationship to obesity [11]. The higher abundance of *Firmicutes* and the lower abundance of *Bacteroides* will contribute to a higher possibility of getting obese. Another example is *Christensenellaceae* which is inversely related to obesity rate. Overall, gut health refers not only to a normal *Firmicutes/Bacteroides* ratio but also to gut microbiome diversity. A diverse gut microbiota population can contribute to sufficient enzyme synthesis, which is responsible for digesting food and producing metabolites. By contrast, an extreme

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imbalance of gut microbiota is referred to as dysbiosis and has pathophysiological consequences. Dysbiosis disrupts homeostasis through a reduction of bacterial diversity and an increased F/B ratio that develops a digestion obstacle, an inflammatory response, and a metabolic profile that is detrimental to gut epithelial health and may finally result in a higher risk of getting obese [12].

3. Gender Differences Related to Intestinal Flora Components

3.1. The Neural Pathway Differences Caused by Microbiota

Obesity has been separated into different types which involves MetS and T2D. MetS has an overall higher prevalence in female population. In addition to that, T2D, another type of obesity has different distribution of age in male and female populations, which may be linked to the hormone secretion [12].

3.1.1. Estrogen level

Estrogen is a kind of hormone which abounds in female's neural system. Some microorganisms like Bacteroides, Escherichia, and Lactobacillus have the gene encoding a substance called β-glucuronidase (GUS), which is an enzyme. The gut microbiota can influence the estrogen level by secreting β-glucuronidase (GUS), which converts conjugated estrogen into deconjugated estrogen in the gastrointestinal tract. It is a crucial step for initiating the down stream signaling and metabolism response. Estrogen is reponsible for regulating the microenvironment including increase glucose level. A decrease in GUS activity will be followed by a reduced deconjugation of estrogen, and thus decreasing the amount of circulating estrogen levels, which can contribute to obesity [13].

3.2. The Dietary Factor and Adipose Tissue

Women tend to store more energy, incorporating free fatty acids (FFA) into triglycerides (TG) at rest and during the post-absorptive state, which contributes to fat storage. It is elaborated that females tend to consume less energy and store fat in their bodies because of their sensitive adipose tissue, which can lead to an increase in storage in adipose tissue [9]. When the adipose tissue cannot hold the fat, it will cause some complications like cardiovascular disease and coronary heart disease. In contrast, men typically have a larger bile acid pool, which aids in fatty acid digestion and helps prevent obesity or overweight by facilitating appropriate fat storage in adipose tissue and avoiding excess accumulation [14]. This metabolic difference leaves women more vulnerable to obesity.

Diets are highly related to the intestinal microbiota, which both pose positive and negative impacts. A Western diet, characterized by high levels of calorie-dense animal meats, refined grains, and sugars, and low levels of fruits and vegetables, negatively impacts gut microbiota. These diets provide little dietary fiber, which can project a huge impact on the intestinal microbiota such as extinction of particular microbiota. This is because Microbiota-accessible carbohydrates (MACs) are widely found in dietary diets and serve as the major energy source of the microbiota. Lack of MACs can destroy the diversity in intestinal microbiota, making a high proportion of fat in the Western diet hard to digest. It is proved that in the mice species, a single generation can recover from reduced gut microbiota diversity, but long-term exposure to low-fiber diets may cause irreversible damage [14]. As women's adipose tissue is more sensitive, they may be more prone to obesity under such conditions.

3.3. Particular Microbiota

In the test of rodents, the sexual hormone has induced symptoms similar to that induced by high-fat-diets, including an increase in the *Firmicutes/Bacteroidetes* (F/B) ratio. Many biological researches

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have suggested that there are many differences in the composition of intestinal flora. In the same study of the Ukrainian statistics, the survey concluded that female has a larger proportion of *Firmicutes* in their intestinal flora, while males have part of the proportion of *Firmicutes* replaced by *Bacteroidetes*. It means that the *Firmicutes/Bacteroidetes* ratio (F/B ratio) of females is significantly larger than that of males and this change will be even more apparent as the age increases. This ratio variance has been found a positive relationship with the obesity rate.

4. Conclusion

The study gives an insight into overall gender differences in obesity prevalence. This variance of gut microbiota in two biological genders influences obesity rate in mainly three ways: gut-microbiota-brain axis, fat or lipids absorption, and specific microbiota ratio. The paper explores how the composition of gut microbiota differs between males and females and how these differences relate to the three pathways, explaining the probable gender inequality in obesity rates. It is proven that women do have a higher probability of getting obese overall due to their physical differences, more specifically, composition differences in gut microbiota. It means female should pay more attention to maintain a healthy living habits to get rid of obesity.

However, there are some factors that can cause a deviation from the truth in the researches. Nowadays, scientists tend to focus on obesity occurrence tendency in gender within specific populations or regions, given the challenges of global data collection. This limitation brings variance by diet preference, inheritance, education level, and other factors. In addition, the composition analysis data is insufficient to represent a precise conclusion. Collecting intestinal flora samples from living humans is particularly challenging due to ethical concerns, as such collection methods may violate human rights in many countries and regions. As a result, much of the research is conducted using rodents (rats or mice) and sometimes primates, which may introduce discrepancies in microbiota composition between species. Even when studies are conducted on humans, factors such as diet, genetics, education, and income level can contribute to variation. Therefore, in the future, it is crucial to process a wider-range survey to minimize the population specificity.

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