Clinical Medicine and Health Research Journal (CMHRJ)
Volume 04, Issue 04, July - August, 2024
Page No. 970-974,

Research Article

Navigating the Complex Nature of Obesity Between Being A Chronic Disease or Personal Responsibility: Have You Betrayed Your Body or Have Your Body Betrayed You?

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Received: 05 June, 2024 **Accepted: 10 July, 2024** **Published: 15 July 2024**

Abstract:

Obesity is a complex multifactorial condition that accumulated excess body fat leads to negative effects on health. Obesity continues to accelerate resulting in a pandemic that shows no significant signs of slowing down any time soon. Raised body mass index (BMI) is a risk factor for noncommunicable diseases such as diabetes, cardiovascular diseases, and musculoskeletal disorders, resulting in dramatic decrease of life quality and expectancy. The main cause of obesity is long-term energy imbalance between consumed calories and expended calories. Here, we explore the biological mechanisms of obesity with the aim of providing actionable treatment strategies to achieve a healthy body weight from nature to nurture. This review summarizes the global trends in obesity with a special focus on the pathogenesis of obesity from genetic factors to epigenetic factors, from social environmental factors to microenvironment factors.

1. Definition of a disease

disease is classically defines as any harmful deviation from the normal structural or functional state of an organism, generally associated with certain signs and symptoms and differing in nature from physical injury. A diseased organism commonly exhibits signs or symptoms indicative of its abnormal state. Thus, the normal condition of an organism must be understood in order to recognize the hallmarks of disease. Nevertheless, a sharp demarcation between disease and health is not always apparent (1).

While the WHO doesn't seem to have a clear definition of disease, it does at least have a definition of health. It is defined as"a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity"(2). Diseases can be classified into: acute and chronic , congenital and acquired , genetic and hereditary , communicable and non communicable (3).

2. Definition of obesity

obesity occur when excess fat accumulation (globally, regionally, and in organs as ectopic lipids) increases risk for adverse health outcomes. Like other chronic diseases, this definition does not require manifestation of an obesity-related complication, simply that the risk for one is increased. This allows for implementation of weight management strategies targeting treatment and prevention of these related conditions. It is important to point out that thresholds of excess adiposity can occur at different body weights and fat distributions depending on the person or population being referenced(4).

Since the 1990s, BMI has been widely used to classify overweight and obesity, both in adults and children. The BMI is defined as the body mass divided by the square of the body height, and is expressed in units of $kg/m^{2.}$ .Major adult BMI classifications are underweight (under 18.5 kg/m^2), normal weight (18.5 to 24.9), overweight (25 to 29.9), and obese (30 or more)(5). However, indirect measures such as BMI, fail to distinguish between fat, muscle or bone mass and are prone to misclassification, particularly among muscular subjects (6). Reliance only on BMI can also lead to misclassification of those with excess body fat, but BMIs corresponding to normal weight. These "metabolically obese but nor- mal weight" . individuals share many health risks with those categorized as obese both based on BMI and %BF . The elevated visceral fat observed in this category is accompanied by increased levels of both liver and muscle fat .In a workplace study, comparing new industry hires from 1990 to 1992 and from 2000 to 2002, there was no significant difference in BMI but a significant difference in %BF, measured by ST (7).

3. Change in the social perception of obesity

The scarcity of food throughout most of human history and consequent connotations that being fat was good and that corpulence and increased "flesh" were desirable are reflected in the arts, literature, and politics of the times. the literary and folkloric stereotypes changed from that of an amiable chubby individual, as reflected in the characterization of Joe by Charles Dickens (1812-1870) as "a wonderfully fat boy," to that of Marty, the hero of the 1953 play by the same name by Paddy Chayefsky (1923-1981), who attributes his rejection by girls to being "an ugly fat man." Thus, before becoming bad, fat became ugly. The consequent passion for slimming continued to mount steadily and reached a frenzy by the middle of the

twentieth century, when the supermodel Twiggy, with her sticklike figure, burst into the fashion scene and became a teenage icon. Still, at the end of every calendar year, we are reminded of the old notion of the jolly fat figure in the person of Santa Claus, in contrast to that of the miserly slim one of Scrooge (8). Most individuals of the western communities view obesity as a negative trait to be avoided .there has beem a cultural prejudice and stigma towards obese people (9).

4. Genetics and obesity

Monogenic obesity is defined as obesity resulting from a mutation or deficiency of a single gene(10). The monogenic forms of obesity known thus far can be divided into three broad categories:

1. Obesity caused by mutations in genes that have a physiologic role in the hypothalamic Leptin-Melanocortin system of energy balance. Specifically, obesity due to leptin, leptin receptor, melanocortin-4 receptor (MC4R), proopiomelanocortin (POMC), and prohormone convertase 1/3 (PC1/3) mutations (11) .

2. Obesity resulting from mutations in genes that are necessary for the development of the hypothalamus. There are three such genes, SIM1, BDNF and NTRK2, with important roles during hypothalamic development, that when mutated lead to severe obesity. These conditions lend more support to the concept that the hypothalamus is critical for energy homeostasis, but the exact mechanisms by which these gene defects lead to obesity are not yet understood (12).

3. Obesity presenting as part of a complex syndrome caused by mutations in genes whose functional relationship to obesity is also not clear such as Bardet-Biedl syndrome, Alstrom syndrome, and Carpenter syndrome, whose etiology has recently been ascribed to the dysfunction of the primary cilium (13). ,however; monogenic obesity is usually a cause of obesity in children and associated with hyperphagia .

5. Obesity and theory of evolution

Essentially, the deposition of fat is an adaptive physiologic process of energy storage that became maladaptive when technological advances altered the balance between the availability of food and the body's expenditure of energy, especially that expended on obtaining food. As such, the story of obesity is indelibly related to that of the history of food. It is a classic example of the diseases that have been argued to be side effects of the evolutionary process.

In the evolutionary history of humankind, body fat seems to have served nature's purpose by outfitting the species with a built-in mechanism for storing its own food reserves. During prehistoric times, when the burden of disease was that of pestilence and famine, natural selection rewarded the "thrifty" genotypes of those who could store the greatest amount of fat from the least amount of the then erratically available foods and to release it as frugally as possible over the long run. This ability to store surplus fat from the least possible amount of food intake may have made survival benefit . Those who could store fat easily had an evolutionary advantage in the harsh environment of early hunters and gatherers (14).

6. Obesity and lifestyle

It is well known that physical inactivity is directly associated with weight gain. Results of studies have demonstrated the relationship between physical activity intensity and abdominal obesity among adolescents (15). Dietary habits (i.e., dietary consumption patterns, meal frequency, skipping breakfast) have been considered key factors contributing to obesity among children and adolescents. Several studies have reported high prevalence of obesity among children and adolescents adopting a diet composed of unhealthy foods such as fast food, sweets and sweetened beverages (16).

7. Obesity as a disease (medicalizing obesity)

As Sadler and colleagues define "'medicalization' as a process by which human problems become defined and treated as medical problems" [17]. Research published within the past few years suggests an explosion in the treatment of conditions that previously had been subjects of "watchful waiting" or nonpharmacologic approaches . Examples of medicalized disorders include menopause, alcoholism, attention deficit hyperactivity disorder (ADHD), posttraumatic stress disorder (PTSD), anorexia, infertility, sleep disorders, and erectile dysfunction (ED) [18].

For example, morbid obesity, which requires surgical treatment, is already recognized as a disease. But medicalization may lower the threshold between what is held as "common" overweight and morbid obesity, increasing the number of people who are viewed as sick. Considering obesity as a disease may therefore have consequences for the individuals affected, society, and the health care system [19].

Medicalization may reduce social discrimination by emphasizing that some of the causes of obesity are outside individual control (20). discrimination on the basis of disease or disability is considered unacceptable, medicalization may advance the rights of the obese .It may also reduce stigma among health care professionals by changing views on etiology . Physicians, who often share the negative biases of society as a whole about obese patients , usually consider the treatment of the causes of illness to be standard medical practice (21).

While medicalization may bring benefits to obese individuals, it will also label all of them "sick," regardless of the rest of their health status . In this way, it might be harmful to those who don't see themselves as ill or who don't try (or want) to lose weight . However, when considered against the effects of widespread and well-documented prejudice, stigmatization, and discrimination ,gains from the medicalization of obesity might offset potential harms (22,23).

8. Obesity as a risk factor for diseases

The long-term risk of type 2 diabetes increases significantly with increasing weight. In the Nurses' Health Study, the effect of weight change on the risk for clinical diabetes was evaluated in 114281 women.[15] After adjusting for age, body weight was the major risk factor for diabetes during a 14-year follow-up. Among women with a 5- to 7.9-kg weight gain, the relative risk for diabetes was 1.9 and for those with an 8- to 10.9-kg weight

gain, the relative risk was 2.7. In contrast, a 5-kg weight loss resulted in a 50% reduction in the risk of diabetes. (24).

Results from the Framingham Heart Study also showed that obesity increases the risk of atrial fibrillation. Among 5282 participants (of whom 55% were women) without atrial fibrillation at baseline, subjects were classified as normal (BMI < 25 kg/m^2), overweight, and obese (BMI ≥ 30 kg/m^2). During a mean follow-up of 13.7 years, a 4% increase in risk of atrial fibrillation/1-unit increase in BMI was observed in men and women after adjustment for cardiovascular risk factors. Compared with normal-weight individuals, in obese subjects the hazard ratio for atrial fibrillation was 1.52 for men and 1.46 for women.(25)

Obesity is an independent risk factor for CVD, defined as including CHD, myocardial infarction (MI), angina pectoris, congestive heart failure (CHF), stroke, hypertension, and atrial fibrillation. Overall, results from large prospective and observational studies confirm the marked adverse effects of obesity on CVD. (26)

Osteoarthritis has a major impact on patient mobility, disability, lost productivity, and patients may become disabled from OA early in life. Obesity is strongly associated with an increased risk of OA of the knee but only a moderate association with OA of the hip has been found. Because OA strongly impacts patient lifestyle and function, it is important to recognize this effect of obesity and the potential need for weight loss and rehabilitation.(27)

Obstructive sleep apnea (OSA) potentially results in a number of complications including pulmonary hypertension, right heart failure, drug-resistant hypertension, stroke, and arrhythmias.(28)

An association between obesity and major depressive disorder (MDD) has long been recognized although a causal association is uncertain. Importantly, many antidepressant drugs are associated with weight gain. The National Epidemiologic Survey on Alcohol and Related Conditions evaluated the relationship between BMI and psychiatric disorders in 41 654 respondents. Among participants, BMI was significantly associated with mood, anxiety, and personality disorders. The odds ratio for a psychiatric disorder was 1.21- to 2.08-fold greater among obese (BMI 30-39.9 kg/m^2) and extremely obese (BMI ≥ 40 kg/m^2) subjects, and the odds ratio for a lifetime prevalence of MDD was 1.53 and 2.02 among obese and extremely obese compared with normal weight subjects.(29).

9. Personal responsibility

Personal preferences determine what, and how much to eat and to exercise, and how important is body shape (aesthetics) to maintaining a healthy lifestyle. No healthy person chooses to go hungry or be malnourished, but there is an element of choice in becoming obese. These issues are closely linked to socio-economic status, culture, and education. Eating should be enjoyable and potentially controllable, but there are often mitigating factors such as the dependability and affordability of the food supply, peer group and advertising pressures. The price of fast food sometimes makes it irresistible. In the U.S., food security among the disadvantaged is cyclical and highest around the time people get their SNAP (Supplemental Nutrition Assistance Program) food stamp dollars. Intake decreases or switches to higher calorie-per-dollar alternatives as the month progresses, when SNAP purchases run out .Such feast/famine cycles of food assistance may paradoxically contribute to unhealthy eating patterns. Unfortunately, medicalization externalizes locus of control ,decreases incentives to change lifestyle behaviors and deters self-management necessary to take active responsibility for weight regulation, noting that intelligence has little to do with self-control (30). There are at least two sides to personal responsibility: medicalizing obesity, which reduces it, and parental supervision, which emphasizes it, since fat children are at high risk for adult obesity

10. Government responsibility

Legislative interventions such as sin taxes and banning soft drink vending machines and junk food advertising to children are all relevant (31).Regressive taxation may be used to benefit the population for whom it is most oppressive. Such tax revenues may go to providing parks, playgrounds, and education programs for disadvantaged children, all of which improve health outcomes. The food industry, which is part of the problem [high-calorie, nutrient-poor, hyper-palatable products (32),must also be part of the solution by encouraging reformulations with healthier ingredients, comprehensible front-of-package food labeling and making price reductions for wholesome foods.

Suitable community-valid interventions can be based on Positive Deviant behaviors of the non-obese living in similar disadvantaged situations (33).There are also Positive Deviant countries such as Japan, Italy, and Switzerland where obesity rates are below 20%.

11. Social role

society must not be judgmental in treating obesity as an individual moral failing or lack of self-discipline and will power. Instead, we have to recognize that patients with obesity are also products of a society of inequality, yet we must not let society “normalize” obesity and also, at the other extreme, “too thin” models. Mis-placed medical and political correctness that leads to hands-off management of obesity, means abrogation of the physician's responsibility: it should not stop recognizing the health problems and consequences and pressing for treatment. For example, some doctors are now even reluctant to raise the issue of obesity lest they be accused of fat shaming by not accepting their patients' proportions (despite the quote at the head of this opinion piece), and thereby receive poor approval ratings in an atmosphere where popularity is equated with good healthcare(34).

12. Pharmaceuticals role

A working drug to help reduce weight in obese patients has long been a dream within many pharma companies. This should be no surprise, given the huge potential such a therapy would have across large parts of the world where a sedentary lifestyle and a high-calorie diet have pushed up belt sizes, and, correspondingly, the size of a potential market (35).Obesity

drugs are a modern day gold rush for drugmakers. Eli Lilly , valued at $347 billion, is close behind $207 billion Novo Nordisk in releasing a weight loss drug, in a market expected to be worth $50 billion by 2030. But the duo's success is enticing rivals and smaller players. That may trigger a wave of dealmaking, and lower returns. Yet a class of drug known as GLP-1 analogues sold by Novo Nordisk and Eli Lilly appears to be almost as good. The U.S. group's Mounjaro, for example, reduced patients' weight by more than 20% in a recent trial. The drugs target receptors in the brain that reduce appetite and help people feel fuller for longer.

Analysts reckon Novo Nordisk's Wegovy drug will bring in nearly $9 billion in revenue by 2030 while Eli Lilly's Mounjaro could generate $21 billion in sales by 2030, according to Visible Alpha. By then, the obesity market could total $50 billion, according to Morgan Stanley. That explains why Novo Nordisk's share price has doubled in the past two years and it trades on 28 times forward earnings, nearly twice the European average. The two leaders may not stay ahead for long. Pfizer , a $276 billion giant, and $206 billion AstraZenec are working on obesity products. And any drugmaker hoping to grab some of the pie could buy up biotechs like $1.4 billion Zealand Pharma or $447 million Altimmune . It helps that the technology behind GLP-1s is already used in diabetes care, making it easier for new entrants to muscle in. Greater competition will drive down prices.(36)

13. conclusion

Obesity is one of the most difficult conditions to manage in healthcare. No-one has found the correct solution because there is no one solution. Comprehensive programs dealing with obesity require coordinated actions at all the nine levels of involvement—national, food system, educational, medical, public health, municipal, societal, parental, and individual. Parental and individual responsibility, choice and self-management clearly have a place near the center of the stage in the obesity tragedy. Otherwise, it is like going to see the play Hamlet and the Prince fails to make an appearance. Individuals are indeed responsible for their health-promoting behaviors but should be held accountable only when they have adequate resources to do so .In conclusion, no one is to be blamed, but everyone has a collective responsibility for working to combat the obesity pandemic—business as usual is no longer an option.

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