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OBESITY - AN EPIDEMIC OF THE 21ST CENTURY – LITERATURE REVIEW

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SUMMARY

Obesity – an epidemic of the 21st century – literature review

Introduction and purpose: The article deals with the problem of obesity, which significantly increases the number of cases among children, adolescents and adults all over the world, leading to the occurrence of systemic disorders. A noticeable increase in the incidence of atherosclerosis, metabolic syndrome and diabetes leads to a reduction in life expectancy. The main aim of the work is to emphasize the seriousness of the contemporary problem, which causes impairment of the functioning of many systems. A secondary goal is to indicate the current standards of obesity treatment and how to deal with overweight.

Brief description of the state of knowledge: Obesity is a disease that affects nearly 800 million people around the world and affects every fourth Pole. Uncontrolled weight gain is caused; lifestyle changes, consumption of highly processed foods, and genetic and endocrine factors. It is a chronic disease with a tendency to relapse, with serious consequences and in need of diagnostics, personalized treatment, and often associated with psychological support.

Material and methods: The article analyzes the research to date and the latest treatment methods, which show that a person struggling with obesity is at risk of over 200 complications, including, for example, fatty liver, stroke, type 2 diabetes or cancer.

Results and conclusion: According to our analysis, obesity is a pathological condition that is truly life-threatening. Despite the society's downplay of the problem, people affected by this disease struggle with many comorbidities that worsen their quality of life.

Keywords: Obesity, Civilization diseases, dyslipidemia,

INTRODUCTION

Obesity and overweight are among the most widespread and perilous civilization threats of the 21st century. The World Health Organization (WHO) defines obesity as the excessive accumulation of body fat in humans, leading to impaired bodily functions and posing a health risk due to increased morbidity and mortality [1]. It is a chronic disease that does not resolve spontaneously and shows a tendency to relapse. Both the WHO and the International Obesity Task Force (IOTF) have established uniform criteria for diagnosing obesity and overweight. The primary component of the assessment is measuring the Body Mass Index (BMI), which is easy to calculate. The equation includes parameters such as body weight expressed in kilograms and height expressed in square meters. It is calculated as the quotient of body weight in kilograms and the square of height in meters. Any BMI value exceeding 30 kg/m² indicates obesity. While BMI is widely used due to its accessibility, considering only 2 parameters, its accuracy remains controversial. It is essential to note that this index is applicable only to adults; therefore, BMI values for children are plotted on centile charts, interpreting the result within a broad or narrow range [2]. This disease causes a deterioration in the quality of life, resulting in health consequences such as non-insulin-dependent diabetes (type II), hyperlipidemia, dyslipidemia, coronary heart disease, myocardial infarction, and sleep apnea [3]. It is the duty of the physician to diagnose and treat

obesity due to its inclusion as a medical condition on the International Classification of Diseases and Related Health Problems list. This requires clinical intervention because of the potential development of conditions such as arterial hypertension, diabetes, cardiovascular diseases, and others [4].

Regardless of the growing promotion of a healthy lifestyle, the number of people with obesity is on the rise. According to the World Health Organization (WHO), over 800 million people worldwide are struggling with obesity [5]. This condition affects individuals of various ages, including children, adolescents, and adults, irrespective of gender, origin, or social class. The issue is not limited to highly developed countries but also extends to developing nations. The prevalence of obesity in Europe ranges from 10-25% in men and 1-30% in women. Over the past 10 years, the incidence of obesity has increased by an average of 20% in most European countries compared to the previous decade [6]. This is linked to the easier accessibility of highly processed products, which are more affordable and, consequently, more frequently chosen and purchased. This ailment does not spare the Polish population

In Poland, in the first half of the 1990s, a comprehensive study called Pol-MONICA was conducted on a large scale, revealing that 45% of the country's residents were overweight [7]. In the diagnostic research conducted on a study group that included patients with overweight and those with normal body weight, namely NATPOL PLUS, it was shown that 47% of Poles are overweight. In a clinical study called LIPIDOGRAM from the year 2004, it was found that 48% of men and 40% of women were overweight [8]. Since then, there has been an observed increase in body weight in a larger population. According to the latest data, approximately one in four residents in Poland is affected by obesity, and over the past few decades, in most countries worldwide, the incidence of overweight and obesity has tripled in the last decade of the 20th century [9]. Based on conducted research, it is estimated that in Europe, about 400 thousand children with excess body weight will emerge each year, with one in five being obese [10]. There is an expectation of a progression in the prevalence of overweight and obesity in our country, currently affecting around 12-14% of children.

ETIOPATHOGENESIS

Etiology of this disease is well understood, irrespective of the significant diversity in causes and pathogenesis; obesity always results from a chronic imbalance in energy equilibrium. The destabilization of energy balance is maintained by an excessive intake of energy disproportionate to its expenditure [11]. Even a small difference between energy

intake from food and energy used for vital functions and daily activities, around <0.5%, leads to weight gain. Obesity often coexists with various metabolic disorders. Elevated levels of triglycerides, LDL cholesterol, and decreased levels of HDL are commonly observed. Additionally, a substantial amount of metabolically active white adipose tissue generates an inflammatory state, which may predispose to insulin resistance [12].

Numerous factors contribute to the development of obesity, including genetic, environmental, psychological, immunological, neurological, and endocrinological factors, in which adipose tissue plays a significant role as an endocrine organ. Environmental conditions exert a considerable influence on uncontrolled weight gain. Lifestyle changes, sedentary work, technological advancements minimizing physical activity, and easy access to high-fat foods and highly processed food are fundamental behavioral factors contributing to an increase in energy balance. All these factors lead to the development of "simple" obesity, which constitutes about 90% of cases and results from a disrupted energy balance [13, 14, 15, 16]. In the times we live in, food has significantly changed its function – once a means of survival, it has now become one of the essential elements of social life and a source of pleasure. An increasing number of people, especially in younger age groups, lose control over the quantity and caloric content of their meals, posing a danger and undoubtedly being the first step towards uncontrolled weight gain. There is no doubt that the causes of the obesity epidemic are highly complex.

METHODS USED TO ASSESS THE SEVERITY OF OBESITY

Obesity can be assessed through the evaluation of the amount of body fat using densitometric, anthropometric, isotopic methods, bioelectrical impedance analysis, or by employing computer tomography with planimetric assessment [17]. These methods are complex, expensive, and often challenging or entirely unavailable. The most popular and rapid means for a general assessment of body mass include indirect measures such as BMI (Body Mass Index), also known as the Quetelet Index, waist circumference measurement (WC), and the Waist-Hip-Ratio (WHR). The collected measures are presented in Table 1.

Table 1. Selected indirect body mass measures [18, 19]

BMI	WC	WHR
Underweight <18,5	Women	Women
Norm 18,5-24,9	<ul style="list-style-type: none"> ▪ Norm <80 cm ▪ Overweight 80cm- 88cm ▪ Obesity >88 cm 	≤ 0,8
Overweight 25-29,9		
Obesity Grade I 30-34,9	Men	Men
Obesity Grade II 35-39,9	<ul style="list-style-type: none"> ▪ Norm 94 cm ▪ Overweight 94cm-102 cm ▪ Obesity >102 cm 	≤ 0,95
Obesity Grade III ≥ 40		

None of these indicators specifies the location of adipose tissue, and this is important information that allows determining to what extent a patient may be at risk of diseases resulting from obesity. Obesity types are identified based on the distribution of adipose tissue, allowing for the distinction of several obesity classifications. Android Obesity—typical in males, abdominal obesity, commonly known as "apple-shaped" obesity, is more dangerous than gluteofemoral obesity — gynecoidal, typical in females, popularly known as "pear-shaped" obesity. Assessing the type of obesity is aided by measuring Waist Circumference (WC) and Waist-Hip Ratio (WHR) because the risk of obesity-related complications decreases as WC decreases [20]. However, this indicator does not describe how fat is distributed in the body. Norms are the same for both genders, but BMI also has its limitations. For instance, weight gain may not be caused solely by an increase in adipose tissue volume but also by muscle mass. The use of this indicator is discouraged for pregnant women, children, individuals over 65 years old, and athletes. [21]

FACTORS AND DISEASES THAT PROMOTE WEIGHT GAIN

One of the most significant environmental factors and the most hazardous is the prevalence of highly processed foods, products that are inexpensive, deeply frozen, and then quickly prepared. Some food products are designed to save time at the expense of unhealthy alternatives filled with high-calorie ingredients [22]. A common cause of the growing obesity

problem among children, adolescents, and young adults is the excessively high glycemic index of food and the increased consumption of beverages containing sugar or its substitutes. According to recent research and epidemiological studies, there is a correlation between the increased consumption of sugary drinks and the accumulation of body weight [23]. High consumption of sweetened beverages is one of the main sources of calories in the diet, responsible for weight gain and related diseases [24, 25]. Excessive weight gain may also be associated with the improper functioning of the endocrine system, hypothalamic tumors, neuroinfections, and the pharmacotherapy used in the treatment of underlying diseases.

The impact of genetics on overweight and obesity is undoubtedly significant. It is believed that genetic factors contributing to obesity account for 25-45% of all obesity causes. Among factors directly related to the disease and predisposing to it, we include conditions such as pseudo-hypoparathyroidism type Ia, Down syndrome, Turner syndrome, Klinefelter syndrome, Prader-Willi syndrome, Alström syndrome, and Cohen syndrome. On the other hand, monogenetic obesity is rare, caused by mutations in single genes such as proopiomelanocortin, melanocortin 4 receptor (MC4R), leptin receptor, and neurotrophic receptor tyrosine kinase 2 [9, 26]. The strongest association with obesity is observed in the FTO obesity susceptibility gene located on chromosome 16 [27]. It is presumed that the FTO gene influences BMI by affecting feelings of fullness and appetite [28]. However, the issue of inheriting a predisposition to obesity in the offspring of obese parents should not be overlooked. It has been shown that there is a 13-fold higher risk of obesity when diagnosed in parents and a 5-fold higher risk in children when the disorder is present in one of the parents [29, 30]. Nevertheless, explaining the development of overweight and obesity in humans solely based on disturbances resulting from genetic mutations should be avoided.

Psychological and neurological factors also deserve attention as they may indirectly contribute to the development of obesity. Stress and an inability to cope with problems are reasons for excessive consumption of high-calorie foods. Predisposing factors to emotional imbalance include depression, anxiety, low self-esteem, leading to abnormal eating behaviors and habits. Obesity may also accompany depression, causing increased appetite and increased sleepiness. It is essential to remember that overweight and increased appetite can be symptoms of depression [9].

CLINICAL CONSEQUENCES OF OBESITY

Patients struggling with obesity are not only fighting to improve their physical appearance, as the destructive impact of this disease is reflected in other organs of the body. The consequences of excessive body weight are so serious that various medical disciplines attempt to combat the disease. Among the most common and dangerous complications are fatty liver disease, type 2 diabetes, stroke, and cancer. Obesity is a disease associated with an increased incidence of other illnesses, disabilities, and premature death. As body weight increases, the risk of developing type 2 diabetes also rises. The occurrence of insulin resistance and obesity is closely related, but not straightforward, as obese individuals often exhibit insulin resistance, while the reverse is not universally true – not all individuals with insulin resistance are obese. Patients with excess body weight have significant adipose tissue reserves, releasing hormones and active substances into the portal circulation [31]. These substances include, among others, Free Fatty Acids (FFA). At the molecular level, clinical studies have shown that FFA can affect insulin action, but it is important to note that this is not the only mechanism considered by scientists.

Cardiovascular diseases are directly linked to preceding obesity. Obesity is a risk factor for ischemic heart disease, responsible for the highest number of patient deaths worldwide. It is also associated with the risk of developing coronary heart disease or a heart attack. Complications of obesity can be noticeable at a young age. The likelihood of developing the disease is not only indicated by BMI values and the amount of adipose tissue but also by its distribution, as abdominal obesity, in particular, is highly dangerous. This condition is the primary predisposing factor for hypertension. According to studies, it is estimated that nearly $\frac{3}{4}$ of hypertension cases in patients in Poland are related to weight gain. Analyzed studies indicate a strong correlation between weight loss and a decrease in blood pressure to values considered normal [32]

The International Agency for Research on Cancer has demonstrated that overweight and obesity increase the risk of developing cancer. Elevated BMI values are associated with an increased incidence of uterine corpus, gallbladder, and ovarian cancers in women, while in men, it is linked to kidney, liver, and colorectal cancers [33].

The excessive accumulation of adipose tissue, as observed in obesity and overweight, is undoubtedly a significant risk factor for the development of gastrointestinal cancer. The processes responsible for inducing carcinogenesis in obese individuals are not fully understood, but it is noteworthy that adipose tissue secretes its own hormones, such as leptin

and adiponectin [34]. Some of the secreted adipokines may act mitogenically on the epithelial cells of the gastrointestinal tract. The carcinogenesis process is based on a chronically ongoing inflammatory process, which promotes the secretion of cytokines such as prostaglandin E2, TNF-alpha, IL-6, and IL-8. Clinical studies indicate that these cytokines are also elevated in obese individuals [35]. The most well-known cancer associated with obesity is colorectal cancer [36]. In the European Investigation Into Cancer and Nutrition (EPIC) study, it was found that in men with high BMI values, the relative risk was 1.55 ($P < 0.006$), with no statistically significant association in women. The conclusion drawn from the results takes into account the distribution of adipose tissue in different genders.

Obesity is a significant risk factor for stroke. In everyday clinical practice, BMI has limited relevance in determining the degree of risk associated with excess body weight. In this context, Waist-to-Hip Ratio (WHR) and Waist Circumference (WC) are more useful. These markers are used adjunctively because they assist in determining the amount of abdominal fat, which exhibits higher metabolic activity than subcutaneous fat. Authors such as Hu, Tuomilehto et al. challenged the conclusion that WHR plays a significant role in assessing the risk of ischemic stroke in women. Statistical analysis revealed that the correlation between WHR and ischemic stroke is observed in males, while in the group of patients with hemorrhagic stroke, no correlation between stroke and WHR was observed in either gender [37].

The National Health and Nutrition Examination Survey III (NHANES III) study demonstrated that girls grappling with obesity at a young age may face difficulties getting pregnant in adulthood [38]. Women are particularly vulnerable to the consequences of obesity. Pregnancy in an obese mother poses advanced perinatal and obstetric challenges. This condition is associated with an increased risk of bleeding during labor and the postpartum period, as well as an elevated risk of peripartum infections.

Among the complications of obesity that should be mentioned are hormonal disorders, gallbladder stones, kidney stones, and an increased susceptibility to respiratory system infections [39].

PREVENTION

In order to prevent obesity and counteract its consequences, the World Health Organization (WHO) has developed recommendations for patients struggling with excess

weight - Dietary Guidelines. The set of recommendations includes positions advocating smoking cessation and increasing physical activity. Undoubtedly, lack of physical activity is not a direct cause of excessive body weight, but introducing movement into life helps in combating it. Patients from the risk group, those with concomitant hypertension, hyperlipidemia, and diabetes, should take special care of themselves and, with the help of their attending physician, implement appropriate pharmacotherapy [40]. The most vulnerable group of patients is children and adolescents, so obesity prevention should be introduced with the utmost care in elementary schools and even in preschools. Parental education has an invaluable impact on combating the disease. Combating obesity is a prolonged process that often requires intervention from specialists in various fields, such as psychiatry, psychology, cardiology, diabetology, and surgery. Specialists warn that weight reduction should not be the sole goal for the patient because changing dietary and lifestyle habits is the only way to lose and maintain a new, lower weight.

TREATMENT

To make a decision about choosing a method of obesity treatment, the overall health of the patient, the stage of the disease, and the causes of its occurrence are taken into account. Treatment goals need to be defined, the patient's commitment assessed, and the opportunity given for acceptance of the proposed therapeutic method. The most common and primary goal of therapy is to reduce the patient's body weight and maintain a healthy weight and dietary habits, thus preventing complications resulting from obesity [41]. Taking into account the coexistence of diseases related to obesity, including diabetes, insulin resistance, dyslipidemia, joint pain, and hypertension, an individualized treatment plan is developed. Treatment is divided into non-pharmacological, pharmacological, and surgical approaches [42]. Treatment begins with non-pharmacological methods, such as proposing a balanced diet aimed at incorporating a large amount of fiber through vegetables, limiting the consumption of red meat, and drinking an appropriate amount of water [43]. Calculating the appropriate caloric balance to be maintained helps determine the quantity and type of meals consumed by the patient. Complementing changes in dietary habits may involve the introduction of plant-based dietary supplements. These supplements have evidence-based efficacy (Evidence-based medicine, EBM). In the treatment of obesity, behavioral-cognitive actions, such as proper diet and physical activity, are crucial, enabling a reduction in LDL cholesterol levels [44].

An important aspect of therapy is pharmacological treatment. If a patient qualifies for such treatment, it should be proposed, with the choice guided by safety and therapeutic effectiveness. Pharmacotherapy is not the primary treatment, so it is used as a complement to non-pharmacological therapy recommendations. Pharmacological treatment is considered for individuals meeting specific BMI criteria and for those who have not achieved $\geq 5\%$ weight loss within 3-6 months. Currently approved anti-obesity drugs by the FDA are specific medications targeting receptors, focusing on reducing energy intake by inhibiting food intake or absorption [45]. In Poland, there are currently three registered drugs for obesity treatment: Liraglutide, Orlistat, and a combination of naltrexone with bupropion [9]. For several years, treatment was limited to Orlistat; however, in 2016, a new drug called Mysimba (a combination of bupropion hydrochloride and naltrexone hydrochloride) was introduced to the Polish market, and it is currently used as a first-line treatment [46].

According to the product characteristics, the combination drug of naltrexone and bupropion is used in the treatment of obesity as an adjunct to a reduced-calorie diet and increased physical activity to reduce body weight in adults (aged ≥ 18 years) with an initial BMI of ≥ 30 kg/m² or ≥ 27 to < 30 kg/m², if accompanied by at least one obesity-related comorbidity (such as type 2 diabetes, dyslipidemia, well-controlled hypertension). The use of this medication is associated with potential side effects, including nausea, headache, dizziness, and insomnia.

The final step in the treatment of obesity is surgical intervention, which does not constitute a definitive cure due to patients' non-compliance with dietary recommendations. Patients are required to change their lifestyle and eating habits [47].

CONCLUSIONS

Obesity is a disease of the 21st century with a complex etiology and pathophysiology influenced by environmental, behavioral, and genetic factors. The prevalence of obesity in Europe has tripled in the last two decades due to lifestyle changes. This condition contributes to increased mortality, a rise in cardiovascular diseases, and leads to depression. Various tools and indicators are used to assess obesity. The most popular, cost-effective, and fastest ones include the Body Mass Index (BMI), Waist-to-Hip Ratio (WHR), and Waist Circumference (WC) or Waist-to-Height Ratio (WHtR). Utilizing all these indicators allows for the most accurate assessment of the risk associated with excessive caloric intake.

Combating obesity is a lengthy process, often requiring a multi-specialist approach, including psychiatrists, psychologists, diabetologists, cardiologists, and in some cases, even surgeons. This process involves implementing appropriate non-pharmacological treatment methods supported by pharmacological treatment. Specialists warn that weight reduction should not be the sole goal for the patient, as changing dietary habits is the primary way to lose and maintain weight in the long run. Therefore, it is valuable to introduce various programs aimed at increasing public awareness regarding diet, caloric content, and food composition. This includes limiting the consumption of fats and simple sugars while simultaneously increasing levels of physical activity.

DISCLOSURE

Author's contribution

Klaudia Kułak: Conceptualization, writing rough preparation, supervision, resources

Katarzyna Kamińska: Writing rough preparation, formal analysis, visualization, data curation

Izabela Sztybór: Methodology, software, check, investigation, writing and editing, project administration.

Project administration: Izabela Sztybór

All authors have read and agreed with the published version of the manuscript.

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The authors deny any conflict of interest

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