Obesity: etiology and the problems it causes

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ABSTRACT

Obesity is one of the biggest health problems today and its prevalence is increasing. It develops with excessive fat accumulation in the body secondary to high energy intake in obesity. It is a chronic disease in which the interaction of genetic, endocrine, metabolic, behavioral, psychological and sociocultural factors plays a role. In addition to endocrine (type 2 diabetes mellitus and insulin resistance, metabolic syndrome, etc.), cardiovascular (hypertension, hyperlipidemia, etc.) and cerebrovascular diseases, diseases such as cholecystitis, sleep apnea, osteoarthritis, hyperuricemia and gout, endometrial, breast, gallbladder cancers in women are associated with diseases such as colon, rectum, prostate cancer in men. These diseases both reduce the quality of life and lead to financial losses in individuals and national economies. Today, preventive health policies aim to reduce morbidity, mortality and economic burden by treating obesity without causing chronic diseases.

Keywords: Obesity, morbid obesity, obesity diagnosis, obesity prevention, body mass index

OBESITY

Obesity, one of the biggest health problems of today, is defined by the World Health Organization (WHO) as an abnormal or excessive amount of fat tissue accumulation that poses a health risk.¹ Although the information about the occurrence of obesity is not complete, it is a chronic disease in which the interaction of genetic, endocrine, metabolic, behavioral, psychological and sociocultural factors plays a role.² Obesity is associated with endocrinological diseases (type 2 diabetes mellitus and insulin resistance, metabolic syndrome, etc.) and cardiovascular diseases (hypertension, hyperlipidemia, etc.), cerebrovascular diseases, cholecystitis, sleep apnea, osteoarthritis, hyperuricemia and gout, endometrial, breast, gallbladder cancers in women, and colon, rectum, prostate cancer in men. It develops with excessive fat accumulation in the body secondary to high energy intake in obesity.³⁻⁵

OBESITY EPIDEMIOLOGY

Obesity is a very common health problem all over the world. According to the estimates of the Non-Communicable Diseases Risk Factor Collaboration (NCD-RisC) Group, the prevalence of obesity in the adult population increased from 3.2% in men and 6.4% in women in 1975 to 10.8% in men and 14.9% in women in 2014.6 According to the Global Burden of Disease (GBD) Obesity Cooperation Group 2015 Report, the obese population in the world has reached 711.4 million (603.7 million adults).⁷ According to WHO statements, in 2016, 39% of adults worldwide were overweight and 13% were obese.8 By 2030, it is estimated that 38% of the world's adult population will be overweight and 20% will be obese. In the US, estimates based on previous lifestyle trends and outcomes indicate that more than 85% of adults will be overweight or obese by 2030.9

The prevalence of obesity in Turkey is increasing day by day as it is worldwide. WHO data report that in 2016, there were 16,092,644 obese individuals in Turkey and Turkey was the country with the highest prevalence of obesity in Europe with a prevalence of 29.5%.4

OBESITY DEFINITION

Obesity is a complex and multifactorial disease that negatively affects health. Since it is not easy to determine the body fat percentage, obesity is defined as excess weight rather than excess fat. 20-25% of the body weight of adult women and 15-18% of men consists of adipose tissue. Increasing the fat distribution above 30% in women and 25% in men causes obesity.4

Considering the fat distribution, there are two types of obesity, android and gynecoid. Android type obesity (central or apple shape obesity) is the type that accumulates hypertrophic fat cells in the abdomen and chest region, is more common in men and has an increased risk of chronic diseases. Gynecoid-type obesity (peripheral or pear shape obesity) occurs with increased fat distribution in the lower parts of the body and hips and is mostly seen in women.¹¹

OBESITY DIAGNOSIS

Methods Used in the Evaluation of Obesity

Neutron activation analysis, underwater weight measurement, total body water, total body potassium measurement (Total Body K40), ultrasonography (USG), computed tomography (CT), deuterium oxide (D 2O), magnetic resonance imaging (MRI), bioelectrical impedance



analysis (BIA), Total Body Electrical Conductivity (TOBEC), single photon absorptiometer (SPA), dual photon absorptiometer (DPA), dual X-ray absorptiometer (DEXA) are included in this group.¹²

Bioelectrical impedance analysis (BIA): Basic principle in the use of BIA; weak electrical current (800 μ A; 50 KHz) is given to the person's body and the permeability is measured using the lowest resistance value of the person formed, lean tissue mass is calculated 2

Indirect (Anthropometric) Methods in the Evaluation of Body Composition

Among the many methods used in the definition and classification of obesity, the most common and most reliable are body mass index (BMI) and waist circumference measurement.¹²

Body mass index (BMI) (kg/m²): BMI is calculated by dividing the body weight in kilograms by the square of the height in meters. Formula: 'BMI= Weight (kg) /Height (m²)' and if this ratio is \geq 30 kg/m², it is considered obesity.¹³ This index, which is the most preferred and easily used today, was first described by Quetelet in 1835. There is a correlation between body fat tissue measured directly by densitometer and BMI that varies according to population.14 The World Health Organization uses the classification made according to body mass index in the evaluation and grading of obesity. According to BMI in adults, underweight, normal and overweight and obesity and their degrees are shown in Table 1.^{4,15}

Table 1 Rating of obesity in adults according to BMI (kg/m ²)		
Underweight	<18.50	
Healthy weight	18.5-24.99	
Overweight	25.00-29.99	
Obesity	≥30.00	
Obesity Class 1	30.00-34.99	
Obesity Class 2	35.00-39.99	
Obesity Class 3 (Extreme)	40.00-49.99	
Super Obesity	≥50.00	

Women and men are diagnosed as overweight and obese based on the same BMI values. Similarly, in the elderly, the height decreases due to osteoporosis, while the muscle mass decreases, the fat ratio increases, and the body fat distribution changes and more fat accumulates around the waist.¹⁶ The validity of BMI measurement points used to diagnose obesity in all adults is doubtful. The term 'Obesity Paradox' in the elderly actually refers to this incompatibility. Unlike other adults, obesity-related morbidity and mortality begin when BMI>33 kg/m² is over seventy years of age. This situation is interpreted as obesity being protective in the elderly. When using the BMI method, it can sometimes be perceived as a fat mass when evaluating people with excess muscle mass such as athletes and cause misconceptions. While the BMI value of the individuals is the same, the amount of body fat is higher in the yellow race than in whites. BMI is actually related to the amount of fat in the body, not the rate of fat. It is possible to calculate body fat from BMI with the formulas' Body fat % (men) = $(1.33 \text{ x BMI } (\text{kg/m}^2)) + (0.236 \text{ x Age } (\text{years})) - 20.2$ and Body fat % (women) = $(1.21 \text{ x BMI } (\text{kg/m}^2)) + (0.262 \text{ x})$ Age (years)) - 6.7 '.17

It is a cost-effective, easy and noninvasive method that is widely used in the evaluation of obesity. The disadvantage is that the distribution of body composition may be insufficient to distinguish between fat and lean tissue. Skinfold thickness measurement (SFT): One of the most commonly used supportive anthropometric methods in the evaluation of body fat is SFT. The thickness of the subcutaneous adipose tissue of the areas (suprailiac, subscapular, biceps and triceps) determined as standard in the body is measured(3). However, the statistical relationships between skinfold thickness and total body fat percent body fat are generally not as strong as BMI.¹⁸

Waist Circumference, hip circumference, waist/hip ratio, waist/height ratio, visceral adiposity index (VAI), neck circumference: The relationship between morbidity and mortality is important according to the localization and distribution of fat tissue instead of the total amount of fat in the body. Another important dimension of obesity is abdominal fat deposition. The amount of intraabdominal (visceral) lubrication is correlated with the waist circumference measurement and the margin of error varies a lot according to the measurement.¹⁹

According to the data of the obesity-lipid metabolismhypertension study group of the Turkish Society of Endocrinology and Metabolism (TEMD), ≥ 100 cm in males and ≥ 90 cm in females were recommended as abdominal obesity criteria (Table 2).⁴

Table 2. Waist circumference values by societies (cm)		
	Male	Female
Europe	≥ 94	≥ 80
USA	≥ 102	≥ 88
Turkey	≥ 100	≥ 90
South Asia and China	≥ 90	≥ 80
Japan	≥ 85	≥ 90
Africa	If there are no va society, Europea	lues belonging to the In data is appropriate
Middle and South America	If there are no va society, South As	lues belonging to the ian data is appropriate

A study of 1898 adult men and 2308 women in 24 centers in all geographical regions of Turkey showed that the waist circumference values that best determine overweight and obese men in adults were 90 cm and 100 cm, respectively, and the values that determine overweight and obese women were 80 cm and 90 cm, respectively.²⁰

Visceral adiposity index (VAI) is a new anthropometric method that indirectly indicates the risk of cardiometabolic complications associated with obesity. Data on safety in patients with acromegaly, diabetes, viral hepatitis C, non-alcoholic fatty liver diseases and polycystic ovary syndrome have been presented.²¹

According to the TURDEP-I study conducted in Turkey between 1997 and 1998, the prevalence of obesity over the age of 20 was found to be 22.3% in both genders; 12.9% in males and 29.9% in females. In the TURDEP-II Study, which was repeated in the same centers, the frequency of obesity was found to be 35.9% (female 44.2%; male 27.3%).²²

According to the Heart Disease and Risk Factors in Turkish Adults (TEKHARF) study, the prevalence of obese people aged 30 and over was 25.3% in men and 44.2% in women, compared to the follow-up of 2001/2002 in Turkey. According to a 1990 survey, the number of obese people had increased by about 90%. Accordingly, it is estimated that 3.2 million men and 5.5 million women have obesity. This shows that the prevalence of obesity has increased by 20% in the last 10 years, regardless of population growth and age.²³

According to the results of the Turkish Nutrition Health Survey (TNHS 2010), the prevalence of obesity and

overweight in adults was reported as 20.5% and 39.1% in men; 41% and 29.1% in women; 30.3% and 34.6% in both genders, respectively. The overall prevalence of morbid obesity was found to be 2.9% (female 5.3%, male 0.7%) (39). When the data from Turkey Population Health Survey (TDHS) conducted on 15-49 year old women published every five years throughout Turkey are examined, it is seen that obesity in women is increasing. According to the results of TDHS 1998, 2003, 2008 and 2013, the incidence of obesity was reported in **Figure 1** as 18.8%, 22.7%, 23.9% and 26.7%, respectively.²⁴



Figure 1. Turkey Population Health Survey (Prevalence of obesity in women aged 15-49 by years (%))

OBESITY ETIOLOGY

It is a multifactorial chronic disease with many genetic, epigenetic, physiological, behavioral, psychological, neurogenic, endocrinological (hormonal), sociocultural and environmental factors in its pathogenesis.²⁵

Genetic Factors

Interactions between the biological environment (genetic/ epigenetic factors) and environmental factors are responsible for the regulation of energy balance and the formation of fat stores.²⁶ Familial inheritance of obesity is the most important supportive condition. In addition, the incidence of obesity in monozygotic twins is higher than in sesquizygotic twins. Individuals in a subgroup in the healthy weight class can maintain their weight with continuous diet and exercise efforts and easily switch to the overweight or obese class by gaining weight when they are not paying attention. In these individuals, depending on the genetic background, metabolic mechanisms work similarly to those in obese individuals, and the term "metabolic obese" has been used for this group in recent years. Researchers have also identified another subgroup, called "healthy obese," which falls into the overweight or even obese class 1 category but is completely normal from a metabolic point of view.⁴

Obesity can be a component of many genetic diseases (such as Prader-Willi syndrome, Laurence Moon Biedl syndrome, Down syndrome, Turner syndrome, Albright's hereditary osteodystrophy, Fröhlich syndrome (adiposogenital dystrophy), hyperostosis frontalis interna). There is rarely a single gene mutation in the genetics of obesity, and obesity is more common as a result of the interaction of many genes with behavior and environmental factors.^{27,28}

Neurogenic and Endocrinological (Hormonal) Factors

It has an inhibitory effect on the satiety center in the ventromedial hypothalamus and the appetite center in the ventrolateral hypothalamus in the brain. Affecting these centers for reasons such as inflammation, trauma or tumor leads to a change in dietary habits and eventually 'hypothalamic obesity'. In addition, many people with hypothalamus lesions or pituitary adenoma extending towards the hypothalamus may develop a tendency to obesity.²⁹

Table 3. Peptides and hormones that affect food intake		
• Appetite Boosters	Appetite Suppressants	
• Ghrelin	• Leptin	
• Galanin	• Glucagon-Like Peptide- 1 (GLP- 1)	
• Neuropeptide Y (NPY)	• Insulin	
• Nitric oxide*	• Corticotropin-releasing factor (CRF)	
• Orexin A-B	• Seratonin	
• Cannabioids*	 α-melanocyte-stimulating hormone (α-MSH) 	
	• Calcitonin	
	• Cocaine-Amphetamine-Regulated Transcript (CART)	
	• Bombesin	
	• Nesfatin-1	
* not in peptide structure		

Obesity develops in people who do not release leptin from adipose tissue due to genetic defect. Hormonal causes of obesity include Cushing's syndrome, insulin resistance, growth hormone (GH) deficiency, insulinoma, hypothyroidism, polycystic ovary syndrome (PCOS), diabetes mellitus (DM), pseudohypoparathyroidism, male hypogonadism, craniopharyngioma and hypopituitarism. Hypothyroidism occurs very often and leads to a decrease in the rate of metabolism and a decrease in energy expenditure. 30,31

Demographic (Age, Gender, Ethnic Origin) Factors

Demographic factors such as age and gender are the unchangeable causes of obesity. As you get older, the muscle tissue and brown adipose tissue in the body decrease and the white adipose tissue increases. As a result of the decrease in physical activity, decrease in basal metabolic rate, change in food intake habits, oxidative stress, hormonal changes and disruption of regulatory mechanisms in the elderly, energy balance is negatively affected and "sarcopenic obesity" occurs. Although it is higher in women, the rate of obesity increases with age in both genders.^{4.31}

Physical Activity

With the developing technology, industrialization and urbanization and the facilitation of lifestyle have caused a decrease in physical activity and daily energy expenditure. As a result of the rapid change in dietary habits, the increase in energy intake has made obesity inevitable. Excessive calorie consumption and sedentary lifestyle are known risk factors for obesity and DM. In the "Let's Eat Healthily, Protect Our Hearts" study conducted with 15,468 individuals over the age of 30 in 7 pilot provinces selected from all geographical regions, it was determined that only 3.5% of people in the society regularly (at least 3 days a week and 30 minutes of moderate-intensity) did physical activity.^{32,33}

Dietary Habits

The second main reason for the increase in the prevalence of obesity is the increase in energy intake as a result of the rapid change in dietary habits. Reduction in physical activity and unhealthy diet are thought to have a share of at least 10% in the global burden of disease.^{34,35}

Psychological Factors

There is a relationship between psychological factors and obesity. Obese individuals have problems with their eating attitudes and have poor quality of life and especially in physical space (self-confidence). It is known that behavioral changes are effective in weight loss. Due to the effects of situations such as stress, depression, sadness and anxiety on hypothalamic centers, changes in appetite, as well as poorly compatible coping response and overeating attitude as a way to get rid of tension are seen. Sleep disorders are also associated with obesity.^{36,37}

Environmental Factors (Sociocultural and Socioeconomic Factors, Drug Use)

It has been revealed that factors such as the environment (place and region of residence), social status, income and education level, number of marriages and births, drug use, and lifestyle contribute to the development of obesity.³⁴⁻³⁷

OBESITY-RELATED PROBLEMS

Metabolic Syndrome and Prediabetes

Obesity has a very close relationship with prediabetes and type 2 DM. Obesity has important implications for morbidity, disability, and quality of life, and like many other health problems, the risk of developing type 2 DM is higher in obese people. According to World Health Organization data, overweight and obesity are responsible for 80% of type 2 DM cases in adults in Europe. The weight distribution of patients with type 2 diabetes mellitus is shown in Figure 2.³⁸⁻⁴⁰



Figure 2. Weight distribution in patients with type 2 diabetes mellitus (%)

Dyslipidemia

One of the common complications of obesity is dyslipidemia, a disorder in lipid metabolism. The increase in the frequency of hypertriglyceridemia in obesity is due to an increase in hepatic TG production due to insulin resistance and hepatic VLDL production due to high carbohydrate consumption and a defect in the lipolysis of triglyceride-rich lipoproteins. With the increase of lipolytic activity in visceral fat tissue, free fatty acids in the portal system increase and cause a decrease in insulin intake to the liver and an increase in the amount of fat. Plasma lipoprotein profile in obese patients is generally high in TG, total cholesterol and LDL cholesterol and low in HDL cholesterol. Dyslipidemia is one of the common metabolic disorders with obesity and its frequency increases in direct proportion to BMI.⁴⁰

Cardiovascular Diseases (CVD) and Hypertension

Studies have shown that obesity is effective in the development of atherosclerosis, symptomatic coronary artery disease, heart failure and atrial fibrillation and is an independent risk factor in the development of CVD. Obesity and atherosclerosis are considered congenital and acquired conditions. Dyslipidemia inflammatory accompanies both atherosclerosis and obesity, and LDL cholesterol and free fatty acids trigger inflammation. Inflammation is a condition associated with obesity, insulin resistance, and type 2 DM, which initiates and accelerates atherosclerosis. Adipocytokines and inflammatory markers released from adipose tissue contribute to atherosclerosis by causing insulin resistance, endothelial dysfunction, hypercoagulability and systemic inflammation. The increase in biomarkers such as Hs-CRP, IL-6 and IL-18 reflects the relationship between obesity-related metabolic disorders and also facilitates the follow-up of treatment.⁴¹

The Framingham Heart Study found that 26% of hypertensive men and 28% of women were overweight or obese. In the "National Health and Nutrition Examination Survey" (NHANES-3) study, it was shown that an excess of 5-9.9 kg increased the risk of developing hypertension in women with a BMI above 25 kg/m², and an excess of 25 kg and above increased the risk by 5.2 times. It has been reported that a weight increase of ten kg causes an increase of 3 mm Hg in systolic blood pressure and 2.3 mm Hg in diastolic blood pressure, which increases the risk of coronary artery disease (CAD) by 12% and the risk of stroke by 24%. In the NHANES-3 study, the frequency of hypertension was found to be around 15% in men and women with a BMI of <25 kg/m², while this frequency increased to 38% in women with a BMI of >30 kg/m² and up to 42% in men.⁴²⁻⁴⁴

Respiratory System Diseases (Obstructive Sleep Apnea Syndrome (OSA), Asthma, Reactive Airway Diseases)

Obstructive sleep apnea syndrome is a condition characterized by recurrent partial or complete upper respiratory tract obstructions resulting in hypoxia/reoxygenation during sleep and is the most important and modifiable risk factor in respiratory system problems associated with obesity. OSA is associated with an increased risk of developing cardiovascular diseases, metabolic diseases, insulin resistance and diabetes. Male gender and obesity are the main risk factors for sleep apnea. In obese patients, lung function abnormalities such as increased lung residual volume, ventilation-perfusion disorders, increased chest wall impedance and bronchospasm, decreased lung compliance and respiratory muscle endurance can be seen as a result of increased diaphragm pressure. In addition, OSA causes a decrease in leptin levels and an increase in ghrelin, thus causing a feeling of hunger and weight gain. Obesity causes OSA and OSA causes obesity, linked in a dangerous vicious circle. A BMI >29 kg/m² increases the risk of OSA by 10 times. The prevalence of OSA is even higher in patients with obesity and diabetes. For OSA, risky people need to be identified and followed up on in terms of complications that may occur. A 10% increase in weight causes a 30% increase in the apnea-hypopnea index (AHI), and a 10-15% decrease in weight reduces AHI by 50%. Therefore, weight loss programs should be added to treatment in all sleep apnea patients who are obese.45

All overweight or obese patients should be evaluated for asthma and reactive airway disease.

Gastrointestinal System and Liver Diseases

The most common are non-alcoholic fatty liver disease (NAFLD), gastroesophageal reflux disease, cholelithiasis, pancreatitis.⁴⁶⁻⁴⁸

Reproductive System Diseases

With obesity, the frequency of polycystic ovary syndrome (PCOS), male infertility (hypogonadotropic hypogonadism), female infertility increases significantly. With the fact that obesity changes hormonal balances, problems such as menstrual irregularities, PCOS, infertility, hirsutism, decreased libido and potency are seen. There is an increase in the secretion of free estrogen and testosterone stored in the adipose tissue, which is increased in obesity. In women with abdominal obesity, androgen production from the ovaries increases directly due to hyperinsulinemia. Lifestyle changes and nutritional treatment are the most important treatments in patients with overweight or obese PCOS. The use of orlistat, metformin or GLP-1R agonists in women with overweight or obese PCOS is effective in promoting weight loss and correcting PCOS findings and providing ovulation. In selected cases, improvement in symptoms and ovulation can be achieved with laparoscopic gastric bypass surgery.⁴⁹⁻⁵¹

Musculoskeletal System Diseases (Osteoarthritis, Carpal Tunnel Syndrome, Osteoporosis)

There are studies showing that obesity reduces the risk of developing osteoporosis as it has positive effects on bone mineral density, bone mass and strength. Increased body weight; degeneration of the cartilage structure secondary to trauma caused by increased load on weight-bearing joints such as knees (most often), hips, spine causes osteoarthritis. Osteoarthritis is also more common in joints such as the hand joint that does not carry a load. The effect of obesity on osteoarthritis is thought to be due to the complex interaction of genetic, metabolic and inflammatory factors, in addition to biomechanical stress. Obesity is effective in developing or progressing low back pain and knee osteoarthritis (OA) in women. The frequency of carpal tunnel syndrome (median nerve neuropathy) has also increased in obese patients.^{52,53}

Psychological Disorders

Mental disorders related to depression, bulimia, sleep disorders, incorrect diet side effects, increased tendency to bad habits, night eating syndrome and perception of appearance are common in obesity. By paying particular attention to the effects of chronic psychosocial stress, exposure to chronic stress can play a role in the development of obesity. Overweight and obese patients should be evaluated for depression and all patients with depression should be recommended. It is not known how much weight loss can improve depression in obesity accompanied by depression.^{54,55}

Cancer

Obesity increases the risk of gallbladder, colon, rectum and prostate cancer in men and gallbladder, ovary, cervical, endometrial and breast cancer in women. Obese patients should be monitored for cancer risk and supported in terms of weight loss.⁵⁶

Anamnesis and Evaluation

When evaluating an obesity patient, the habits of the person, the social environment in which he/she lives, the history of obesity, previous weight loss attempts, the factors involved in etiopathogenesis and accompanying comorbid diseases, his/her expectation and compliance with treatment, etc. should be considered. Appropriate environment and conditions should be provided for the ideal evaluation and physical examination of obese patients. Evaluation of patients should be performed in clinics with sleep apnea monitors, psychologically evaluable, hormonal and molecular genetics laboratories. A comprehensive history, physical examination and laboratory evaluation of the patient's obesity should be performed. It is recommended to study obesity-related blood tests (fasting blood glucose, HbA1c, fasting lipid profile, liver enzymes, renal function tests (creatinine, blood urea nitrogen), uric acid, TSH) and general laboratory tests (hemogram, complete urine analysis) in each obese patient. If necessary, additional examinations and evaluations such as glucose tolerance test, abdominal ultrasonography, dexamethasone suppression test or 24-hour urinary cortisol or 23:00 at night salivary cortisol, prolactin, estradiol, FSH, LH, pregnancy tests, androgens, apolipoprotein B and/or lipoprotein particle count, cranial CT or MRI, resting electrocardiogram (ECG), cardiac stress tests, echocardiogram can be performed. However, the measurement of insulin resistance in patients with excess weight and obesity has no clinical meaning and benefit in terms of diagnosis, treatment plan and follow-up. Since patient motivation and compliance with treatment are the most important elements of weight control programs, they should be questioned using a visual scale or some guided questions.1,2,4,38

CONCLUSION

Today, obesity, which is the second most important cause of preventable deaths after smoking, is a complex and multifactorial disease that negatively affects our health and causes disorders and diseases in many systems in the body. First of all, approaches to prevent the development of obesity should be emphasized as a society. Early diagnosis, early intervention and reduction in the prevalence of obesity will not only provide people with a healthy life, but also prevent many conditions that may develop, preventing obesity will prevent great economic losses as well as mental and physical benefits.

ETHICAL DECLARATIONS

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