REVIEW ARTICLE

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# "UNRAVELING OBESITY: A COMPARATIVE EXPLORATION OF PATHOPHYSIOLOGY, HORMONAL REGULATION, AND ASSESSMENT WITH RESPECT TO UNANI AND CONVENTIONAL MEDICINE PERSPECTIVES"

Unani Medicine

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## ABSTRACT

Obesity is a significant global health challenge with escalating prevalence rates and profound public health implications. In conventional medicine, obesity results from an imbalance between calorie intake and expenditure, exacerbated by environmental, genetic, and socio-economic factors. Hormonal factors like leptin, insulin, and neuropeptide Y play crucial roles in appetite regulation and energy balance, while in Unani medicine, obesity, termed Saman-e-Mufrat, is attributed to disturbances in innate heat and excess coldness affecting the Rooh, leading to vascular constriction and increased morbidity risks. Assessment methods discussed include Body Mass Index (BMI), waist circumference, and imaging techniques like CT and MRI. Understanding these diverse perspectives on obesity is essential for developing effective prevention and management strategies, particularly in addressing its complex interplay of biological, social and environmental factors.

## KEYWORDS

Obesity, Saman-e-Mufrat, BMI, Hormonal Regulation in Obesity

## INTRODUCTION

Obesity poses a significant public health challenge, directly and indirectly contributing to numerous health conditions, exacerbating health inequalities, and leading to premature death. Since 1975, the global obesity prevalence has tripled [1].

If current trends persist, it is projected that by the year 2030, around 38% population of the global adult will be overweight, with an additional 20% classified as obese [2].

Obesity is currently recognized as the fifth leading cause of death worldwide. According to the World Health Organization (WHO), obesity is characterized by " excessive or abnormal accumulation of fat that may impair human health." The WHO also clarify further that "the primary reason of overweight as well as obesity is an imbalance of the energy i.e between calories consumed and calories expenditure." [3,4]. Over the past twenty years, obesity rates have surged across developing nations. Researchers in their study estimate that the number of obese adults rose dramatically from 105 million in 1975 to 641 million in 2014, highlighting a concerning trend [5,6].

Obesity is emerging as an important health problem in India. The National survey on Family Health shows that 12.1% men and 14.8% women in India are either overweight or obese[7].

In the developing country India, the population of obese adults increased from 24.1 million in 2012 to 32.8 million in 2016 [8].

### Methodology

#### Search strategy

Data collection involved searching various electronic databases including PubMed, Scopus, DOAJ, Wiley Online Library, Springer Link, Science Direct, MDPI, NCBI and Google Scholar, Index copernicus. The search followed PRISMA guidelines [9] and used predefined keywords: "obesity" or "Hormonal regulation in obesity" or "Investigations to be done in obesity" along with their equivalents in different languages: "Saman-e-Mufrat", "Afraate Farbahi", or "Motapa". This approach ensures comprehensive retrieval of relevant articles, facilitating thorough research exploration in the field.

### Unani Medicine and Obesity

In Unani medicine, obesity is referred to as Saman-e-Mufrat, a term derived from two words: "Saman," meaning fat, and "Mufrat," meaning excessive, various unani Authors also uses the term Motapa, Afraate Farbahi also in context of Obesity [10].

Saman-e-Mufrat concept behind the term was first introduced by the scholar Buqrat (Hippocrates: 460-370 BC) in his renowned book "Fasool e Buqratia." He provided a comprehensive description of Saman-e-Mufrat (obesity), detailing its complications, prevention and management. Another Unani physician, Rofus (98-171 AD), in the book "Tahzeel Sameen" (Treating Obesity), explained that obese individuals are more susceptible to diseases due to a deficiency of Khoon Saleh (healthy blood) and an excess of Khilt e Bhalgam (Phlegmatic humour) [11]

Saman-e-Mufrat is associated with increased mortality, as described by the esteemed scholar of Unani Jalinoos (Galen: 129-210 AD). He noted that obese individuals are more likely to experience early deaths as compared to lean and thin individuals [12].

Ali Bin Rabban Tabri (700-780 AD) detailed the underlying factors and pathophysiology of Siman Mufrit in his renowned work, Firdousal Hikmat [13].

Daud Antaki (1541-1599 AD) discussed complications and treatments for obesity in his book "Tazkira tu Uolil Albab." Azam Khan (1813-1902 AD) provided detailed descriptions of treatments for Saman-e-Mufrat in "Rumuz-e-Azam." [14]

### Pathophysiology of obesity in unani medicine

According to renowned Unani scholars, in Saman-e-Mufrat, Hararat-e-Ghareezia (innate heat) is severely compromised due to increased Buroodat (coldness). This excess Buroodat leads to vasoconstriction, causing narrowing and contributing to the obstructed propagation of Rooh (vital spirit) in the body [15].

According to Jalinoos the term given to Obesity is 'zakhamat-e-jism' with reference to him Rhazi translated his quote as " A person obese from childhood died earlier than a normal person"[16].

Rabban Tabri stated that the primary contributors to obesity are overindulgence in food and a lack of physical activity[17].

Ibn-e Nafis stated that morbid matters hinder the absorption of Akhlat (humors), resulting in narrowing and hardening of blood vessels due to the accumulation of Laham (meat) or Shaham (fat). This produces a turbulance in the flow and penetration of Rooh (vital spirit) into the various organs [18].

At various times, this congestion and narrowing are caused by increased levels of Shaham (fat) and Balgham (phlegm) in the blood vessels leads to increased pressure which may lead to the rupture of the blood vessels anywhere in the human body, As, the vessels of the heart and brain (vital organs) being particularly vulnerable. Due to which the patient may develop severe zeequn nafas (dyspnea) and khafqan (palpitations) [19, 15,16].

When Rooh (vital spirit) fails to meet the body's requirements, tissues become hard and blood flow is not adequately maintained to the heart and brain. Consequently, the patient may suffer from syncope, stroke and in some severe cases sudden death may occur [19].

Pathomechanism of obesity according to conventional medicine

The development of obesity in a person is influenced by the regulation of calorie usage, appetite control and physical activity levels. However, it also involves complex interactions with the accessibility of healthcare systems, socio-economic status and inherent genetic along with environmental factors.

### Nutritional Intake, Energy Balance and Environment

Food intake and expenditure of energy both of them are regulated by numerous interconnected and overlapping pathways. These processes revolve around the communication pathways linking the brain with peripheral tissues, such as adipose tissue and the gut. Enteric sensory pathways regulate energy intake, leading to vagal afferent signaling and endocrine cascades that activate brain regions responsible for appetite and feeding behavior. Many of these same pathways also moderate energy expenditure. Approximately 70% of total expenditure of energy is due to resting metabolic rate, which is closely linked to fat-free mass. The remaining expenditure of energy is due to the thermogenic effect of food and physical activity. Hormonal and neurological pathways play significant roles in mediating these aspects of expenditure of energy and may be influential in obesity[20,21].

The primary causes of obesity are still a topic of debate. Present health guidelines for managing obesity focus on the fundamental physiological principle that fat accumulation results from an imbalance between calorie intake and expenditure. The obesity epidemic has largely been exacerbated by the increased consumption of highly palatable and energy-dense foods. Additionally, diet, along with various social, economic, and environmental factors related to food availability, significantly impacts an individual's ability to maintain energy balance [22].

Marketing strategies that promote sugary and high-fat foods and beverages can negatively influence human behavior. These advertisements often enhance the preference for energy-dense foods and high sugar drinks [23].

Further research work is necessary to comprehend the root cause of these trends and to identify strategies to address social inequities and their role in obesity contribution.

### Hormonal Regulation in Obesity

#### Leptin

Leptin, a proteinicious hormone composed of around 167 amino acids, secreted by white adipose tissue(i.e adipokine). Its circulating levels are directly proportional to body fat mass. Leptin functions by promoting satiety and increasing expenditure of energy. It achieves this by activating proopiomelanocortin (POMC) neurons and inhibiting neurons that express neuropeptide Y (NPY) in the hypothalamus. Genetic alteration in the leptin gene or its receptor can lead to deficiency in leptin signaling, results in hyperphagia which leads to severe obesity in humans. This underscores the pivotal role of intact leptin regulation in maintaining normal weight [24].

An alternative proposition suggests that leptin potentially plays a key role in preventing the loss of body fat rather than in reducing fat accumulation. In this scenario, only when leptin levels fall below the threshold necessary for appetite inhibition does it become significant, while elevated leptin levels do not further decrease energy intake [25]. Additional research is required to comprehensively understand role of leptin's involvement in obesity.

#### Insulin

Insulin, secreted by β-cells of pancreas, also shows a positive correlation with body weight and adipose tissue mass, serving as a negative feedback signal to the central nervous system. Similar to leptin, elevated levels of insulin lead to a reduction in food intake. Obesity commonly correlates with insulin resistance and high blood sugar levels, conditions widely believed to be driven by elevated free fatty acids level , which in turn lead to hyperinsulinemia[26].

Numerous studies have indicated that elevated insulin secretion may play a role in the obesity development. This is achieved by promoting fatty acids uptake and glucose by adipocytes and encouraging the storage of calories as fat, while simultaneously inhibiting lipolysis[25].

#### Neuropeptide Y

Neuropeptide Y (NPY), a 36-amino acid neuropeptide, plays a pivotal role in various physiological processes within both the central and peripheral nervous systems. It is one of the most influential regulators of feeding behavior and energy homeostasis and is abundantly expressed in the central nervous system. In the brain, NPY is produced in the arcuate nucleus and serves as the most potent short-term stimulant for appetite [24].

NPY is synthesized by neurons within the sympathetic nervous system, where it promotes vasoconstriction and the expansion of fat tissue. During periods of negative energy balance, hypothalamic NPY levels increase, stimulating greater food consumption while simultaneously reducing energy expenditure, largely through the inhibition of sympathetic nervous system activity [27].

#### Ghrelin

Ghrelin is synthesized by cells that are spread across the gastrointestinal tract , with the highest concentration found in the stomach's fundus. In the hypothalamus's arcuate nucleus, ghrelin activates neurons similar to those affected by NPY [26,28]

There by increasing appetite. Moreover, ghrelin also prompts the release of growth hormone [29].

Therefore, the impact of ghrelin stimulation may vary depending on the broader hormonal environment, complicating the establishment of a direct association with obesity.

#### Secretin

Secretin (SCT) is a peptide hormone made up of 27-amino acid and is secreted by S-cells from duodenum in response to acidic conditions, primarily recognized for its role in stimulating bicarbonate secretion in the pancreas. Interestingly, SCT also has anorectic properties, meaning it can reduce appetite, without causing conditioned taste aversion. This effect is mediated both peripherally, through vagal activation, and centrally.

When SCT levels increase in response to feeding, it activates thermogenesis in brown adipose tissue by stimulating lipolysis through binding to secretin receptors on brown adipocytes. This activation is detected by the brain, leading to a feeling of satiation. While research into SCT's role in regulating food intake has been ongoing for several years, further studies are needed to explore its potential for therapeutic applications[30,31].

#### Cholecystokinin

CCK is secreted by mucosal enteroendocrine cells of the jejunum and duodenum, neurons from the enteric nervous system, and the brain is the prototype of a satiety hormone [32].

The presence of food in the gut lumen stimulates the secretion of cholecystokinin (CCK), which in turn leads to the termination of a meal [33].

CCK activates vagal afferent neurons, which transmit gastrointestinal signals to hindbrain regions, including the nucleus of the solitary tract [34].

Some of these hindbrain neurons project to the parabrachial nucleus, a central hub for appetite regulation. Various stimuli related to food intake, such as gastric distention and the secretion of CCK or glucagon-like peptide 1 (GLP-1), activate calcitonin gene-related peptide-expressing neurons (CGRPPBN) in the parabrachial nucleus, leading to the physiological termination of a meal[35].

Hypothalamic AgRP neurons inhibit CGRPPBN neurons, suggesting that AgRP stimulation promotes feeding partly by suppressing CGRPPBN neuron activity[35].

Activation of these neurons has also been implicated in the rapid onset of severe, life-threatening anorexia [36]. Because hypothalamic AgRP neurons inhibit (CGRPPBN) neurons, AgRP stimulation appears to promote feeding, in part, by suppressing the activity of (CGRPPBN) neurons[35]. While POMC neurons play a physiological role in limiting food intake over extended periods, CCK-stimulated

(CGRPPBN) neurons act as an acute brake on food consumption during individual meals [25].

**Incretin Hormones**

Incretin hormones, which are peptides secreted by specialized enteroendocrine cells located at various levels of the gut, play a crucial role in regulating insulin secretion in response to food intake. The primary incretin hormones identified are glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1). They significantly enhance the secretory response of insulin when glucose orally ingested, as compared to when it is intravenously administered. This amplified response is known as the incretin effect. Besides their role in stimulating insulin secretion, it also influence the release of glucagon. Specifically, glucose-dependent insulinotropic polypeptide (GIP) promotes glucagon secretion. GLP-1 inhibits glucagon secretion, particularly at lower glucose concentrations, serving as a mechanism to regulate blood sugar levels particularly at high glucose levels[37, 38].

GLP-1 also exerts significant impacts on various organ systems. Notably, it reduces appetite and intake of food, resulting in sustained weight loss over a span of time. Both hormones also elicit various additional effects in adipose cells, bone, and the cardiovascular system[39,40] .

**Amylin**

Amylin is produced by pancreatic beta cells and is co-secreted alongside insulin [41].

It is also found in the lateral hypothalamus, where it synergistically interacts with leptin to decrease energy intake [42].

Amylin works in tandem with leptin in the arcuate nucleus to influence satiety. However, it is the area postrema in the hindbrain that plays a vital role in mediating this satiating effect[43].

In this context, amylin enhances cGMP levels and phosphorylates ERK, which are signals that initiate the anorexic effect [44,45].

**Antioxidants**

Low concentration of various antioxidants, including antioxidant fat and water soluble vitamins like Vit C, Vit E and glutathione, have been linked with obesity[46].

Additionally, obesity is also associated with increased oxidative stress caused by macrophages releasing proinflammatory cytokines. This imbalance in the redox state disrupts lipid and carbohydrate metabolism by promoting insulin resistance [47].

**Assesment Of Obesity**

In large epidemiological studies and clinical settings, body weight and anthropometric measurements are used commonly to estimate body fat and its distribution. These methods are quick and cost-effective for assessing body fatness. In contrast, smaller scale studies, like clinical trials, often utilize densitometry or imaging techniques to measure body fat more precisely.

**Methods for Assessing Obesity**

**Body Mass Index (BMI)**

For BMI(wt/$h^2$), weight (wt)in kg and height in meter, wt should be measured using digital scales. Ideally, patients should be weighed with bare feet and light clothing, preferably fasting and after voiding the urine. Height is measured using a stadiometer (regularly calibrated). Patients should stand barefoot with their feet together, ensuring the head is aligned with the Frankfort plane, an imaginary line from the lower border of the eye orbit to the auditory meatus [48].

In 1993, the World Health Organization (WHO) convened an Expert Consultation Group tasked with establishing standardized categories for BMI (Body Mass Index). Their findings were subsequently documented a technical report in 1995 [49].

The WHO established four distinct categories based on BMI (Body Mass Index): underweight, normal weight, overweight, and obese. Under this classification, individuals are categorized as underweight if their BMI falls between 15 and 19.9, normal weight if it ranges from 20 to 24.9, overweight if it ranges from 25 to 29.9, and obese if it is 30 or higher.

According to findings using linear regression, a BMI of 16.9 in men and 13.7 in women is indicative of a complete absence of body fat stores [50].

**Waist circumference (WC)**

Waist circumference (WC) is an indicator of central or abdominal obesity and can be used to diagnose obesity. According to the World Health Organization (WHO), a WC greater than(>94 cm) in men and greater than (>80 cm) in women is linked to an elevated risk of metabolic complications. This risk becomes much higher with a WC exceeding 102 cm in men and 88 cm in women. For Asian populations, the cut-off values are lower, with a WC greater than (>90 cm) in men and greater than (>80 cm) in women.

Measuring WC is straightforward and avoids considering the hips, which include bone and skeletal muscle in addition to fat. The correct method for measuring WC involves placing the tape measure midway between the lower ribs and the iliac crest [48,51].

**Hip circumference (HC)**

Hip circumference (HC) is taken at the widest part over the greater trochanters using a narrow, non-stretchable, flexible tape. The measurement should be performed while the individual is standing and at the end of a exhalation.

**Waist-hip ratio (WHR)**

The waist-hip ratio (WHR) is calculated by dividing the waist circumference (WC) by the hip circumference (HC), ensuring the same units of measurement are used for both [48].

WHR is a simple and effective way to measure of central obesity, predicting the likelihood of various health issues associated with excess abdominal fat. According to the World Health Organization (WHO), a WHR of at least 0.90 in men and 0.85 or higher in women classifies as abdominal obesity. A ratio exceeding 1.0 for either sex signifies a significantly elevated risk of health complications. WHR is a quick, cost-effective, and accurate method for assessing a patient's adiposity and potential risk for cardiometabolic disorders [52].

**Body fat percentage**

In recent years, bioelectrical impedance analysis (BIA) has emerged as a more precise method for assessing body composition. Bioelectrical impedance vector analysis (BIVA) has proven effective in evaluating nutritional status and hydration levels. According to the National Institutes of Health Technology Assessment Conference Statement on BIA for body composition measurement, BIA provides a more accurate estimation of comparative fat mass than BMI [53].

The Endocrine Society of India defines obesity as having a body fat percentage exceeding 25% in men and 30% in women[52].

**Densitometry**

Total body fat was traditionally assessed using densitometry, which applies Archimedes' principle of water displacement. This method assumes two main body compartments: fat, with a density around 0.7 g/ml, and fat-free tissue, with a density approximately 1.0 g/ml. According to this principle, if two individuals of equal weight on land have differing proportions of body fat and lean tissue, the individual with higher body fat and lower lean tissue will weigh less underwater. This method helps estimate body composition based on the difference in weight between dry and submerged conditions[48].

**Imaging Techniques**

Recent advances in imaging technology, such as computed tomography (CT) and magnetic resonance imaging (MRI), now enable the visualization of discrete deposits of body fat. These techniques allow for the assessment of specific fat depots, including visceral fat, which correlates more closely with metabolic abnormalities compared to subcutaneous fat. However, quantifying fat in other structures like the liver or muscles remains challenging. Despite its benefits like Accurate and precise estimations of regional fat mass. Imaging is costly and may pose difficulties for individuals with claustrophobia.

## CONCLUSION

Addressing the global obesity epidemic requires a multifaceted approach that integrates insights from both conventional and traditional medicine systems. Efforts should focus on promoting healthy lifestyle choices, enhancing nutritional literacy, addressing socioeconomic disparities, and advancing medical research to develop personalized interventions. By combining modern scientific knowledge with traditional wisdom of Unani medicine, physicians can better combat obesity and its associated health risks, fostering a healthier future for populations worldwide.

### Conflict of interest

The Authors declares that they have no conflicts of interest to disclose.

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