Original Research Article

The Egyptian Journal of Immunology

The Egyptian Journal of Immunology,
E-ISSN (2090-2506)
Volume 32 (4), October, 2025
Pages: 101–109.
www.Ejimmunology.org
https://doi.org/10.55133/eji.320412

Multisystem effects of obesity: dysregulation of leptin, thyroid hormones, autoantibodies, immune and neurological responses

Rusul A. A. Alshammary[1], Assal G. Alshammary[1], Wijdan M. Hameed[2] and Abdullah S. Al-Karawi[1]

[1]Department of Microbiology, College of Science, Mustansiriyah University, Baghdad, Iraq.
[2]Department of Chemistry, College of Science, Mustansiriyah University, Baghdad, Iraq.

Corresponding author: Rusul A. A. Alshammary, Department of Microbiology, College of Science, Mustansiriyah University, Baghdad, Iraq.
Email:
rusulabood.mc.s.zoo.2020@uomustansiriyah.edu.iq

Abstract

Many changes occur in the levels of hormones, thyroid autoantibody, and some immune and neurological factors in people with obesity. It appears that these changes are a result, not a causes, of obesity. This research aimed to know the effect of obesity on the levels of leptin, leptin receptor, immunological marker, thyroid hormones, thyroid autoantibody and neurological marker. This study involved 80 participants aged 20-60 years. Of these, 40 were obese with BMI ≥30 and 40 with normal weight. Serum samples were collected for the analysis Leptin, soluble leptin receptor (SLEP-R), interleukin (IL-6), tumor necrosis factor (TNF)-α, Thyroid-Stimulating Hormone (TSH), free Triiodothyronine (FT3), free Thyroxine (FT4), thyroid autoantibody (TG-ab and TPO-ab) and neurological markers [Brain derived neurotrophic factor (BDNF), nerve growth factor (NGF), and noradrenalin (NA)]. There was a notable significant increase in leptin, but the level of SLEP-R decreased. While there was a significant increase in the level of IL-6, TNF-α, TSH, FT3, TG-ab, TPO-ab and NGF in obese patients. Also, there was significant decrease in FT4, BDNF and NA levels in obese patients compared to the control group. In conclusion, obesity is not just excess fat storage. It is associated with impaired leptin signaling, and an inflammation condition that affect the immune system, which cause changes in thyroid hormones and an increased risk of autoimmunity disorders.

Keywords: Obesity, leptin, thyroid hormones, thyroid autoantibodies, neurological and immunological markers.

Date received: 19 August 2025; **accepted:** 02 October 2025

Introduction

Obesity is a chronic neurobehavioral disease that relapses, progresses, and can be treated, influenced by multiple factors. Increased body fat results in dysfunction of adipose tissue and abnormal physical forces stemming from fat mass, which adversely impacts metabolic, biomechanical, and psychological health.[1] The World Health Organization (WHO) defines obesity as an excessive amount of body fat that can adversely affect health.[2] It is important to note that if a person's weight increased significantly above average, they are considered obese. Weight gain refers to an increase in body weight that is above normal but not to the extent of obesity [3]

Obesity chiefly occurs attributable to consuming extra calories than the body burns during daily actions and exercise. Additionally, genetic issue, ecological circumstances, hormones, and levels of metabolism affect it.[4] A number of factors play important roles to obesity, particularly extreme expenditure of high-sugar foods, and high fat, which has high energy. Even little quantities of these foods have an important sum of calories that eventually cause weight gain. Lacking of exercises, physical activity and increased office work will lead to storing the energy as fat.[5] Certain hormones have correlation with health issues, for example Cushing's syndrome that can raise the obesity risk; other examples include polycystic ovary syndrome (PCOS) and hypothyroidism.[6] Obesity may develop from frequent diseases; for instance, heart disease, diabetes mellitus, variety of cancers, mental health challenges and musculoskeletal issues.[7] The main method for assessing obesity is throughout body mass index (BMI), by which individual's height and weight were measured. BMI reflects content of fats in the body of adults.[8]

One of the first discovered substances, produced from adipose tissue is leptin, which released by white adipose tissue and one of the adipokines. Over two decades ago, leptin and its receptors that distributed throughout the body, was identify as key regulators of energy and body weight equilibrium. It has a role in several physiological processes, including reproduction. Serum leptin levels monitor energy balance in adipose tissue and communicate this information to the brain. Leptin production, secretion, and receptor binding regulate hunger and energy expenditure through several hormones and neurotransmitters. Previous studies demonstrated that obesity defined by BMI was the strongest predicator of high leptin level.[9] Following secretion, it binds to its receptor, leptin receptor (LEP-R). The LEP-R distribution amplifies the pleiotropic effects of leptin and is vital for regulating body mass through a negative feedback loop involving adipose tissue and the hypothalamus. Pharmaceutical companies are investigating leptin-based drugs for weight loss treatment.[10]

The role of adipokines in the pathophysiology of immune-mediated illnesses is highly supported by clinical and experimental studied.[11] Interleukin (IL)-6 is a pro-inflammatory cytokine that regulates inflammation responses. In obesity, the excess of macronutrients in adipose tissues triggers the generation of inflammatory adipocytes like IL-6 and tumor necrosis factor α (TNF-α), resulting in a chronic inflammation state in obese individuals. This increase in IL-6 and TNF-α in obesity can lead to cardiovascular complications, and insulin resistance.[12]

Recently, studies are focusing on the correlation between body weight and thyroid function. While it is widely acknowledged that hypothyroidism is associated with weight gain and hyperthyroidism with weight loss, there remains debate about how thyroid function alters in cases of obesity. However, testing thyroid hormones is often necessary when investigating the root cause of obesity.[13] Thyroid gland's roles in the body encompass raising the basal metabolic rate and augmenting the number of calories required for the body to operate while at rest. It regulates calorie-burning processes and influences the balance between fat storage and breakdown within the body, tailored to the individual's metabolic condition.[14] Concurrently; there has been an increase in the incidence of autoimmune diseases, such as thyroid autoimmunity in obese individual. There may be a connection between obesity and autoimmunity, since recent research has indicated that obesity may raise the risk of autoimmune conditions such rheumatoid arthritis, psoriatic arthritis, and inflammatory bowel disease.[15]

Brain derived neurotrophic factor (BDNF) is essential for maintaining energy homeostasis and controlling food intake. Its lower levels in obese people can cause hyperphagia and weight gain which may result from increased hunger and decreased satiety.[16] BDNF would send several signals to a section of the hypothalamus responsible for food intake, causing a feeling of fullness.[17] Recent research has demonstrated that nerve growth factor (NGF) is a true adipokine as it is directly produced by human and mouse adipocytes in cell culture. NGF affects the immunological and endocrine

systems in addition to peripheral and central nervous cells. Additionally, a favorable correlation was found between peripheral NGF levels and a few circulating markers of inflammation that are frequently overproduced in obese patients.[18] Therefore, it is possible that slow alterations in noradrenalin impact eating habits and metabolism, potentially contributing to obesity; however, this has not yet been thoroughly examined in vivo in people.

The aim of this study was to investigate the frequency of serum leptin level, leptin receptor, thyroid hormones level, thyroid autoantibody, cytokines and neurotransmitters among Iraqi adult with obesity.

Materials and Methods

Subjects

This study, involved 80 female participants, comprising 40 patients classified as obese (BMI ≥30) and 40 controls with normal weight. All participants were aged between 20 and 60 years. The obese patients (BMI <30 kg/m²) were randomly chosen from visitors of Medical City Hospital and Al-Kindi Hospital.

Samples were collected over three months (from December 2024 to February 2025). All participants underwent weight and waist circumference measurements. Weight was divided by the square of height (kg/m2) to determine body mass index (BMI). Each participant provided information regarding age, gender, duration of illness, medication and nutrition adherence, smoking status, and any existing medical conditions.

Samples Collection

Peripheral venous blood samples (5 ml) were drawn using a sterile syringe. Following collection, blood samples were placed in a gel activator tubes and permitted to coagulate for 15 minutes at 40°C. Subsequently, samples were centrifuged at 1200 xg for 10 minutes to isolate the serum. The serum then put into sterilized plain tubes and stored at -20°C. This serum was utilized for assessing levels of Leptin, soluble Leptin receptor (SL-R), immunological markers, IL-6 and TNF-α. Thyroid-Stimulating Hormone (TSH), free triiodothyronine Hormone (FT3), free thyroxine hormone (FT4), the thyroid autoantibody, thyroglobulin antibodies (TG-ab) and thyroid peroxidase antibody (TPO-ab). Neurological marker Brain derived neurotrophic factor (BDNF), nerve growth factor (NGF) and noradrenalin (NA) were assed.

The levels of leptin and SLEP-R were determined using the sandwich enzyme-linked immunosorbent assay (ELISA) kits, obtained from Shanghai YL Biont, China, according to the manufacturer's instructions.

Thyroid hormones and thyroid autoantibodies were tested using chemiluminescence immunoassays on a Cobas 601 analyser (Roche Diagnostics), according to the manufacturer's instructions.

The sandwich ELISA technique was used to determine BDNF, NGF, NA, IL-6, and TNF-α, utilizing commercially available kits (Melsin – China), according to the manufacturer's instructions.

Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS, version 20). Acquired data underwent T-tests to compare study groups. Correlation coefficients were estimated between parameters. Results are presented as means with descriptive statistics. *P* value of ≤ 0.05 was considered significant.

Results

Table 1 displays the Age, Body Mass Index (BMI), total body fat percentage (TBF%), and waist hip ratio (WHR) among obese individuals. The findings indicated a significant increase in BMI, TBF% and WHR among obese patients (35.53±0.73 kg/m^2, 36.53±9.07 and 0.84±0.07, respectively) when compared to controls (24.57 ± 0.78 kg/m^2, 23.65±5.02 and 0.67±0.066, respectively) (p<0.001).

Table 1. Levels of Age, body mass index (BMI), total body fat (TBF), and waist hip ratio (WHR) in all study groups.

Groups	Age (Years) (mean ±SE)	BMI (kg/m^2) (mean ±SE)	TBF% (mean ±SE)	WHR
Obese individuals	36.37±1.98	35.53±0.73	36.53±9.07	0.84±0.07
Controls	30.10±2.34	24.57 ± 0.78	23.65±5.02	0.67±0.066
p value	0.0001	0.0001	<0.0001	0.0004

$p \leq 0.05$ is significant.

Table 2 reveals significant increase in the levels of leptin in obese patient in comparison with the control group (1.318±0.162 vs 0.521±0.135 ng/ml, respectively) (p<0.001), while the soluble leptin receptor (SLEP-R) showed a significant decrease in obese patients compared to the control group (5.841±0.476 vs 7.766±1.010 ng/ml, respectively) (p<0.001).

Table 2. Serum levels of Leptin and soluble leptin receptor (SLEP-R) in obese and control groups.

Group	Leptin (ng/ml) (mean± SE)	SLEP-R (ng/ml) (mean ±SE)
Obese	1.318±0.162	5.841±0.476
Control	0.521±0.135	7.766±1.010
p value	0.0001	0.0001

$p \leq 0.05$ is significant.

In table 3; the level of TNF-α, and IL-6 was significantly increased in obese (60.70± 3.84 and 89.65±5.9 pg/ ml, respectively) when compared with the control group (41.88± 0.694 and 50.38±3.6 pg/ ml, respectively) (p<0.001).

Table 3. Serum levels of tumor necrosis factor α (TNF-α) and Interleukin (IL)-6 in the control and obese groups.

Group	TNF-α (pg/ml) (mean ±SE)	IL-6(pg/ ml) (mean ±SE)
Obese	60.70± 3.84	89.65±5.9
Control	41.88± 0.694	50.38±3.6
p value	0.025	0.0012

$p \leq 0.05$ is significant.

Table 4 reveals significant increase in the levels of TSH (mlU/ml) and FT3 (nmol/l) among obese individuals compared to the control group (3.83±1.21 mlU/ml and 2.87±0.40 pmol/l, respectively, vs. 1.88±0.36 mlU/ml and 1.72±0.45 pmol/l, respectively) (p<0.001). Conversely, there was a significant decrease in the level of Free Thyroxine Hormone (T4) (nmol/l) among obese individuals (14.07±0.94 pmol/l) compared to the control group (18.79±0.56 pmol/l) (p<0.001).

Table 4. Serum Thyroid-Stimulating Hormone (TSH), free Triiodothyronine (T3), and Free Thyroxine Hormone (T4) levels in the obese and control groups.

Group	TSH (mlU/ml) (mean ±SE)	FT3 (pmol/l) (mean ± SE)	FT4 (pmol/l) (mean ±SE)
Obese	3.83±1.21	2.87±0.40	14.07±0.94
Control	1.88±0.36	1.72±0.45	18.79±0.56
p value	0.0004	0.0068	0.0001

$p \leq 0.05$ is significant.

Table 5 shows the levels of thyroid antibodies, there was a significantly increase in the level of TG-AB and TPO-AB in obese patient (55.7 ±10.8 and 92.4 ±15.7 AU/ml, respectively), in comparison with the control group (30.9 ±7.6 and 12.5 ±6.1 AU/ml, respectively) (p<0.001).

Table 5. Serum Thyroid-Stimulating Hormone (TSH), Triiodothyronine (T3), and Thyroxine Hormone (T4) levels in the obese and control groups.

Group	(TG-AB) AU/ml (mean ±SE)	(TPO-AB) AU/ml (mean ±SE)
Obese	55.7 ±10.8	92.4 ±15.7
Control	30.9 ±7.6	12.5 ±6.1
p value	<0.001	<0.001

$p \leq 0.05$ is significant.

Table 6, shows the level of neurological markers (BDNF, NGF and NA). The level of NGF was significantly increased in the obese subjects when compared to the control group (11.83±1.2 vs 6.90±0.62 ng\ml) (p<0.001). While there was significantly decrease in BDNF and NA levels in obese patients (0.154±0.1 and 87.04±2.39 ng\ml, respectively) in comparison to the control group (0.461±0.14 and 119.27±4.5 ng\ml, respectively) (p<0.001).

Table 6. Serum neurotrophins, brain derived neurotrophic factor (BDNF), nerve growth factor (NGF), and noradrenalin (NA) in the control group and the obese group.

Groups	BDNF ng\ml (mean ±SE)	NGF ng\ml (mean ±SE)	NA ng\ml (mean ±SE)
Obese	0.154±0.1	11.83±1.2	87.04±2.39
Control	0.461±0.14	6.90±0.62	119.27±4.5
p value	0.0001	0.0001	0.024

$p \leq 0.05$ is significant.

Discussion

One worldwide health concern is obesity. By 2030, studies predict that 57.8% of people worldwide would be overweight or obese. The WHO reports that, worldwide, people who are overweight or obese die at a higher rate than people who are underweight.[17] The mechanisms that lead to weight gain in particular the biological underpinnings that leads to overeating are only partially understood.

By stimulating the leptin receptor (LEP-R)–signal transducer and activator of transcription 3 (STAT3) signaling pathway in a subset of hypothalamic neurons, the protein hormone leptin, which is generated from adipocytes, promotes hunger and energy homeostasis.[19] The present investigation found that the leptin level in obese patients was significantly higher than in the control group. While the level of leptin receptor was significantly decreased in obesity patients compared to the control group.

This may indicate leptin resistance, according to Gruzdeva et al., 2019, who found that an abnormality in intracellular signaling linked to obesity causes development of leptin resistance.[20] Thus, the cause of elevated leptin level in obese people is that the anorexic effects of leptin decreased despite an increase in its concentration in obese individuals. [20] In this study, because the increase in the level of leptin in the obese individual and decrease of leptin receptor expression suggested that there is a leptin resistance in obese individual. This observation agreed with a previous study, demonstrated that obesity impaired the effect of leptin action and causes leptin resistance. Leptin resistance is caused by its failure to reach target cells, reduced expression of LEP-R, or disruption of LEP-R signaling. Several mechanisms lead to leptin resistance including mutation in genes that include leptin and its receptor.[11, 19] Ob gene (an adipose specific gene) transcription, directly affects leptin levels, which correspond with adipocyte size and fat content. It is unknown how these variables interact and change pathways to cause leptin resistance. This could be influenced by external factors such as dietary habits, and the expression of leptin modulated by circadian rhythms which hmay contribute to leptin resistance. Another study demonstrated that leptin resistance could result from diminished transport across the blood-brain barrier. Short truncated forms of LEP-R are expressed in micro capillaries at the Blood-Brain Barrier (BBB), providing leptin to the neurological system. Moreover, high plasma leptin concentrations can cause a decrease in BBB permeability.[11]

Leptin, like other acute phase reactants, stimulates the release of inflammatory cytokines such IL-6, IL-12, and TNF-α. Exposure to inflammatory stimuli like TNF-α and IL-1 enhances leptin expression in adipose tissue and circulating leptin, leading to a feedback loop that promotes inflammation. This feedback loop highlights the role of leptin in promoting low-grade inflammation by increasing the production of pro-inflammatory mediators and acute phase reactants, which can lead to chronic inflammation. [9] This finding agreed with the result in the current study in which there is significantly increase in the level of IL-6 [12] and TNF- α[21] in obese individuals. Another study showed that there was significantly increase in IL-6 in 60 obese individual.[12] Increased IL-6 receptor expression in the hypothalamus suggests that it may have a function in modulating hunger and energy intake.[12]

The main driver behind the onset of obesity is an imbalance between energy expenditure and intake. Thyroid hormones play a crucial role in regulating energy utilization by controlling metabolic rate, thermogenesis, and cellular respiration. The relationship between thyroid hormones and obesity involves various interactions. Both the mass and functionality of adipose tissue are intricately regulated by thyroid hormones and TSH. [13] The present study reveals a notable increase in the levels of TSH and T3, accompanied by a significant decrease in the level of T4.

Swarnalatha et al., 2017 studied diet in an animal model; the food was rich in carbohydrates and fat. They observed an important increase in the levels of T3 and TSH during the first five months causing elevation in the level of TSH in individuals with a notable obesity, this may be resulted from stimulation of thyroid glands. Leptin is supposed to be the major driver that causes the increases in the level of TSH in obese individuals[22] this was in line with our result. Fat accumulation increases TSH secretion because of a resetting of the hypothalamic-pituitary operated by the adipose tissue, however, this elevation may not signify authentic hypothyroidism. The increase in TSH and subsequently T3 levels might be seen as the body's protective response to prevent weight gain. Moreover, the notable conversion of T4 to T3 in obese individuals was suggested as a protective mechanism to prevent fat accumulation due to heightened energy expenditure.[23]

Obesity correlates with a heightened risk of various autoimmune diseases, such as autoimmune thyroiditis. A recent study showed that obesity was significantly associated with TG-Ab and TPO-AB and TG-Ab was more prevalent in obese people.[24] Such outcomes agreed with our results since there was significantly increase in TG-Ab and TPO-AB in

obese individuals than in the control group. It is unknown how autoimmune illness and obesity are related. Studies indicated that adipokines could be an essential in immunological diseases.[25] The immunological and inflammatory responses are mediated by adipokines, such as IL-6 and leptin. Adipose tissue is essential for maintaining human immunological function.[26] Thyroid autoimmunity is linked to adipokine dysfunction. Leptin which was shown to influence the immune system and enhance the production of TPO-Ab by reorienting the balance of T helpers toward the phenotype of T helper 1 cells and preventing regulatory T cells from functioning.[11]

In a cross section study, included 108 Saudi adult obese individuals, demonstrated significantly a decrease in BDNF in the serum of obese individual, this result agreed with the current study result.[17] This protein plays a complex role in the body since a lack of it is linked to increased body weight, which causes its external administration to enhance energy expenditure and decrease food intake. [16] Exogenous BDNF administration and BDNF gene transfer in a mouse model of obesity and type 2 diabetes mellitus restored normal food intake, causing weight loss and lowering insulin resistance.[27] In contrast, another research found no differences in the levels of blood BDNF protein between two groups of 14 healthy subjects, non-obese controls, and 24 obese individuals.[28] The discrepancy between previous studies and our findings might be caused by variables including smoking, sex, age, food consumption, exercise, and ethnicity that may have an impact on BDNF readings.[17]

Our study found that the level of NGF was significantly higher in patients with obesity than in those with normal weight. The findings are consistent with a previous study that found that the serum levels of NGF were higher in the obese group than in the control group. [29] There are few studies on the association of NGF with obesity. However, the mechanism underlying this increase due to NGF contributes to inflammation, and persistent inflammation in adipose tissue is a hallmark of obesity. Moreover, NGF may result from inflammation in obese adipose tissue or be directly linked to adipose tissue malfunction.[30] Another in vivo study showed that high NGF also had higher levels of free fatty acids and blood triglycerides. Higher levels of NGF are associated with increased hepatic triglyceride secretion, likely due to the up-regulation of hepatic lipoprotein secretion, suggesting that NGF may play a role in pathways related to energy metabolism and body weight.[31] This could be another explanation for the role of the NGF in obesity.

In addition to neurotrophins, a research on mice demonstrated that obesity can cause adipose tissue's sympathetic innervation to be disrupted, which lowers noradrenaline level.[32] Also, a prior study showed that a higher body mass index is associated with decreased noradrenalin availability in the hypothalamus as well as modifications to a network that mediates emotional well-being.[33] The result of our study showed a significantly decrease level of noradrenalin level in obesity patient when compared with the control group. Numerous processes, such as disturbed sympathetic innervation, changed metabolism, and modifications in receptor sensitivity, might cause obesity to lower noradrenaline levels. To date, there are no recent studies on the role of obesity in affecting norepinephrine levels. Therefore, new research is required to determine the reason and mechanism behind this effect.

In conclusion, in many cultures, obesity has spread like wildfire, leading to major issues with both public health and the economy. In addition, it is linked to higher rates of illness, death, and a shorter lifespan. This study demonstrated that any changes in the expression of leptin and its receptor result in leptin resistance, which contributes to obesity-related complications. The Observation of novel whole-body leptin regulatory mechanisms could facilitate the creation of new treatments for leptin resistance. The current study suggested that leptin may play a role in thyroid autoimmunity by enhanced autoantibody thyroid injury. In addition, the increase in the levels of T3 and TSH accompanied with decrease in levels of T4, may explain the mechanism the body's defense next to gain in weight. In

addition, this study indicated a possible connection between autoimmune thyroid illness and obesity. High levels of IL-6 and TNF-α may indicate chronic and systemic inflammation associated with obesity. This could result in the onset of atherosclerosis and coronary heart disease. There is some evidence that the BDNF, NGF, and NA may be implicated in obesity. A BDNF deficit causes a person to not feel full, which contributes to the development of obesity. Obesity could be a potential risk factors for neuropathy. These findings underscore the significance of monitoring these biomarkers for metabolic syndrome risk and highlighting the need for targeted interventions in the Iraqi individual to mitigate the health impacts of obesity, which could aid in the development of obesity management strategies.

Acknowledgements

The authors express their gratitude to all participants in this study for their resources, which contributed to enhancing the quality of this work.

Author Contributions

RAAA, Made substantial contributions to the conception and design of the study, methodology development, data collection, data analysis, and drafting of the manuscript. AGA, Contributed to the literature review, data interpretation, validation of findings, and critical revision of the manuscript for important intellectual content. WMH, Performed statistical analyses, prepared figures and tables, and contributed to the writing and interpretation of the results. MA, Assisted in material preparation, data collection, and data analysis. All authors have read and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) denies receipt of any financial support for the research, authorship, and/or publication of this article.

Ethical approval

The protocol of the study was reviewed and approved by the scientific Research Ethics committee of the Mustansiriyah university (approval number: BCSMU/1224/00065 Z).

Informed consent

An informed consent was obtained from each subject before being included in the study.

References

1. Fitch A K, Bays H E, et al. (2022). Obesity definition, diagnosis, bias, standard operating procedures (SOPs), and telehealth: an Obesity Medicine Association (OMA) *Clinical Practice Statement (CPS)* 2022. Obesity Pillars, 1, 10000

2. Ahmed S K, Mohammed R A. (2025). Obesity: Prevalence, causes, consequences, management, preventive strategies and future research directions. *Metabolism Open*, 100375..

3. Shariq O A, & McKenzie T J. (2020). Obesity-related hypertension: a review of pathophysiology, management, and the role of metabolic surgery. *Gland surgery*, 9(1), 80.

4. Romieu I, Dossus L, Barquera S, et al. Working Group on Energy Balance and Obesity. (2017). Energy balance and obesity: what are the main drivers?. *Cancer causes & control*, 28(3), 247-258.

5. Kasman M, Hammond R A, Mack-Crane A, et al (2023). Using agent-based modeling to extrapolate community-wide impact from a stakeholder-driven childhood obesity prevention intervention: Shape Up Under 5. *Childhood Obesity*, 19(2), 130-138.

6. Ali L Q, Alshammary R A, Alshammary A G, et al. (2024). A hormonal side effect of anabolic steroids among a sample of Baghdad male bodybuilders. *Steroids*, 209, 109465.

7 Chooi Y C, Ding C, & Magkos F. (2019). The epidemiology of obesity. *Metabolism*, 92, 6-10.

8. Francesco C, Toselli S, Mazzilli M, & Coratella G. (2021). Assessment of body composition in athletes: A narrative review of available methods with special reference to quantitative and qualitative bioimpedance analysis. *Nutrients*, 13(5), 1-25.

9. Obradovic M, Sudar-Milovanovic E, Soskic S, et al. (2021). Leptin and obesity: role and clinical implication. *Frontiers in endocrinology*, 12, 585887.

10. Alshammary A G., Ali L.Q, El-Haboby B T, et al. (2024). Effects of 5% Coca-Cola consumption on metabolic, renal, and hepatic markers in adult Balb/c mice. *International Journal of Design & Nature and Ecodynamics*, Vol. 19, No. 6, pp. 2091-2096.

11. Baranowska-Bik A, & Bik W. (2020). The Association of Obesity with Autoimmune Thyroiditis and Thyroid Function-Possible Mechanisms of Bilateral Interaction. *International Journal of Endocrinology*, 2020(1), 8894792.

12. El-Mikkawy D M, EL-Sadek M A, EL-Badawy M A, et al. (2020). Circulating level of interleukin-6 in relation to body mass indices and lipid profile in Egyptian adults with overweight and obesity. *Egyptian Rheumatology and Rehabilitation*, 47(1), 7.

13. Walczak K, & Sieminska L. (2021). Obesity and thyroid axis. I*nternational journal of environmental research and public health*, 18(18), 9434.

14. Sawicka-Gutaj N, Zawalna N, Gut P, et al. (2022). Relationship between thyroid hormones and central nervous system metabolism in physiological and pathological conditions. *Pharmacological Reports*, 74(5), 847-858.

15. Zynat J, Li S, Ma Y, et al. (2020). Impact of Abdominal Obesity on Thyroid Auto-Antibody Positivity: Abdominal Obesity Can Enhance the Risk of Thyroid Autoimmunity in Men. *International Journal of Endocrinology*, 2020(1), 6816198.

16.Pandit M, Behl T, Sachdeva M, et al. (2020). Role of brain derived neurotropic factor in obesity. *Obesity Medicine*, 17, 100189.

17. Taha M A, Al-Maqati T N, Alnaam Y A, et al. (2022). The association between brain-derived neurotrophic factor (BDNF) protein level and body mass index. *Medicina*, 59(1), 99.

18. Samario-Román J, Larqué C, Pánico P, et al. (2023). NGF and its role in immunoendocrine communication during metabolic syndrome. *International journal of molecular sciences*, 24(3), 1957.

19. Saxton R A, Caveney N A, Moya-Garzon M D, et al. (2023). Structural insights into the mechanism of leptin receptor activation. *Nature Communications*, 14(1), 1797.

20. Gruzdeva O, Borodkina D, Uchasova E, et al. (2019). Leptin resistance: underlying mechanisms and diagnosis. Diabetes, metabolic syndrome and obesity: *targets and therapy*, 191-198.

21. Eswar S, Rajagopalan B, Ete K, et al. (2024). Serum tumor necrosis factor alpha (TNF-α) levels in obese and overweight adults: correlations with metabolic syndrome and inflammatory markers. *Cureus,* 16(7).

22. Swarnalatha N B, Roy N, Gouda M M, et al. (2018). High-fat, simple-carbohydrate diet intake induces hypothalamic–pituitary–thyroid axis dysregulation in C57BL/6J male mice. *Applied Physiology, Nutrition, and Metabolism*, 43(4), 371-380.

23. Longhi S, & Radetti G. (2013). Thyroid function and obesity. *Journal of clinical research in pediatric endocrinology*, 5(Suppl 1), 40.

24. Yan Y, Xu M, Wu M, et al. (2022). Obesity is associated with subclinical hypothyroidism in the presence of thyroid autoantibodies: a cross-sectional study. *BMC endocrine disorders*, 22(1), 94.

25. Song R H, Wang B, Yao Q M, et al. (2019). The impact of obesity on thyroid autoimmunity and dysfunction: a systematic review and meta-analysis. *Frontiers in immunology*, 10, 443404.

26. Clemente-Suárez V J, Redondo-Flórez L, Beltrán-Velasco A I, et al. (2023). The role of adipokines in health and disease. *Biomedicines*, 11(5), 1290.

27. Motamedi S, Karimi I, & Jafari F. (2017). The interrelationship of metabolic syndrome and neurodegenerative diseases with focus on brain-derived neurotrophic factor (BDNF): Kill two birds with one stone. *Metabolic brain disease*, 32(3), 651-665.

28. Lommatzsch M, Zingler D, Schuhbaeck K, et al. (2005). The impact of age, weight and gender on BDNF levels in human platelets and plasma. *Neurobiology of aging*, 26(1), 115-123.

29. Bulló M, Peeraully M R, Trayhurn P, et al. (2007). Circulating nerve growth factor levels in relation to obesity and the metabolic syndrome in women. *European Journal of Endocrinology*, 157(3), 303-310.

30. Kawai T, Autieri M V, & Scalia R. (2021). Adipose tissue inflammation and metabolic dysfunction in obesity. *American Journal of Physiology-Cell Physiology*, 320(3), C375-C391.

31. Nonogaki K, Moser A H, Shigenaga J, et al. (1996). β-Nerve Growth Factor as a Mediator of the Acute Phase Responsein Vivo. *Biochemical and biophysical research communications*, 219(3), 956-961.

32. Esler M, Straznicky N, Eikelis N, et al. (2006). Mechanisms of sympathetic activation in obesity-related hypertension. *Hypertension*, 48(5), 787-796.

33. Hesse S, Becker G A, Rullmann M, et al. (2017). Central noradrenaline transporter availability in highly obese, non-depressed individuals. *European journal of nuclear medicine and molecular imaging*, 44(6), 1056-1064.