

PALA, Katarzyna Maria, TOMASZEWSKA, Wiktoria, SIUDZIŃSKI, Paweł, ŁYKO, Mateusz, SKOCZYŁAS, Alicja, GOLIŃSKA, Maria, NOWAK, Anna, KURASZ, Jakub, PODLASIEWICZ, Wiktoria, DUDZIAK, Piotr and MAJ, Wojciech. The Hormonal dysregulation and its consequences in Obese Women - overview. *Journal of Education, Health and Sport*. 2025;77:56907. eISSN 2391-8306.

<https://doi.org/10.12775/JEHS.2025.77.56907>

<https://apcz.umk.pl/JEHS/article/view/56907>

The journal has had 40 points in Minister of Science and Higher Education of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of 05.01.2024 No. 32318. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical culture sciences (Field of medical and health sciences); Health Sciences (Field of medical and health sciences).

Punkty Ministerialne 40 punktów. Załącznik do komunikatu Ministra Nauki i Szkolnictwa Wyższego z dnia 05.01.2024 Lp. 32318. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu). © The Authors 2025;

This article is published with open access at Licensee Open Journal Systems of Nicolaus Copernicus University in Torun, Poland Open Access. This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author (s) and source are credited. This is an open access article licensed under the terms of the Creative Commons Attribution Non commercial license Share alike.

(<http://creativecommons.org/licenses/by-nc-sa/4.0/>) which permits unrestricted, non commercial use, distribution and reproduction in any medium, provided the work is properly cited.

The authors declare that there is no conflict of interests regarding the publication of this paper.

Received: 11.12.2024. Revised: 10.01.2025. Accepted: 20.01.2025. Published: 30.01.2025.

Hormonal dysregulation and its consequences in Obese Women - overview

Katarzyna Pala [KP] University of Opole plac Kopernika 11A, 45-040 Opole

ORCID: 0009-0004-0787-3872

e-mail: kaspal109@gmail.com

Wiktoria Tomaszewska [WT] University of Opole plac Kopernika 11A, 45-040 Opole

ORCID: 0009-0005-6166-1659

e-mail: wiktomaszewska@o2.pl

Paweł Siudziński [PS] University of Opole plac Kopernika 11A, 45-040 Opole

ORCID: 0009-0002-4476-9412

e-mail: pawelsiudzinski99@gmail.com

Mateusz Łyko [ML] University of Opole plac Kopernika 11A, 45-040 Opole

ORCID: 0009-0009-2530-2789

e-mail: matlyk@wp.pl

Alicja Skoczylas [AS] University of Opole plac Kopernika 11A, 45-040 Opole
ORCID:0009-0002-2185-5406
e-mail: alicjasko1999@gmail.com

Maria Golińska [MG] University of Opole plac Kopernika 11A, 45-040 Opole
ORCID: 0009-0008-2772-6131
e-mail: maria.golinska99@gmail.com

Anna Nowak [AN] University of Opole plac Kopernika 11A, 45-040 Opole
ORCID: 0009-0005-8833-1107
e-mail: anulla1008@gmail.com

Jakub Kurasz [JK] University of Opole plac Kopernika 11A, 45-040 Opole
ORCID: 0009-0004-3955-1552
e-mail: jakubkurasz30@gmail.com

Wiktoria Podlasiewicz [WP] Wrocław Medical University wybrzeże Ludwika Pasteura 1,
50-367 Wrocław
ORCID: 0009-0001-6578-5297
e-mail: wiktoria.podlasiewicz@student.umw.edu.pl

Piotr Dudziak [PD] University of Opole plac Kopernika 11A, 45-040 Opole
ORCID: 0009-0000-6173-740X
e-mail: piotr-dudziak@outlook.com

Wojciech Maj [WM] University of Opole plac Kopernika 11A, 45-040 Opole
ORCID: 0009-0003-2869-3718
e-mail: Rottel45@gmail.com

Abstract

Introduction

The article focuses on the multidimensional consequences of obesity in women, particularly regarding hormonal dysregulation and its impact on metabolic and reproductive health. The authors emphasize that obesity and overweight are global health challenges, with an increasing influence on women's health. According to the World Health Organization (WHO), obesity is defined as a BMI greater than 30 kg/m², and current trends indicate a rising prevalence of this issue, generating significant health and economic costs.

Aim of Study

The aim of this study is to review the literature on the impact of obesity on hormonal balance in women and analyze the associated health issues, such as polycystic ovary syndrome (PCOS), insulin resistance, infertility, and cardiometabolic diseases. The authors strive to identify key mechanisms of dysregulation, which are crucial for proposing potential treatment directions and preventive strategies.

Material and Methods

A review of scientific literature published between 2000 and 2024 was conducted, utilizing databases such as PubMed. From these, 34 peer-reviewed articles were selected, focusing on women with obesity and examining the effects of hormonal dysregulation on health. The analysis covered key mechanisms, including adipokine dysfunction, such as leptin and adiponectin, and their impact on glucose metabolism, lipid regulation, and appetite control. The PRISMA criteria were applied to ensure the high quality of the selected studies.

Analysis of the Literature

Obesity leads to chronic inflammation, which disrupts hormonal functions, including insulin regulation, sex hormones, and the hypothalamic-pituitary-adrenal axis. Women with obesity are more likely to experience ovulatory disorders, reduced oocyte quality, and impaired

endometrial receptivity, significantly affecting fertility. Decreased insulin sensitivity, hyperandrogenism, and leptin resistance are central mechanisms underlying these disorders.

Conclusion

The review highlights the necessity of a multidimensional approach to treatment, encompassing lifestyle modifications, pharmacotherapy (including GLP-1 agonists), and surgical interventions in severe cases. The authors suggest that future research should focus on personalized strategies tailored to the individual needs of patients. A comprehensive approach can not only alleviate the symptoms of obesity but also improve the quality of life for women by reducing the risk of metabolic and reproductive complications.

Keywords: Obesity, Hormonal dysregulation, Insulin resistance, Adipokines, Leptin, Adiponectin, Polycystic ovary syndrome (PCOS), Reproductive health, Metabolic health, Cardiometabolic diseases, Infertility, Hyperandrogenism, Psychological health, Chronic inflammation, Lifestyle interventions, Pharmacotherapy, Bariatric surgery, Health disparities, Women's health,

Introduction

Obesity and overweight represent some of the most pressing health challenges of the contemporary world, gaining increasing significance in the context of women's health. According to the World Health Organization (WHO), overweight occurs when the body mass index (BMI) exceeds 25 kg/m², while obesity is diagnosed when BMI is 30 kg/m² or higher [1, 2]. BMI, as a straightforward measure of body weight relative to the square of height, serves as a practical tool for assessing overweight and obesity in populations. Currently, nearly two in five adults globally are living with overweight or obesity, with substantial implications for public health, healthcare systems, and economic resources [2].

Background

The global prevalence of overweight and obesity has risen dramatically, underscoring the multifactorial and chronic nature of these conditions. In 2019, the economic cost of obesity was estimated at 2.19% of the global gross domestic product (GDP), with projections suggesting that this burden could rise to 3.29% by 2060 [1, 2]. In low- and middle-income countries (LMICs), the economic impact is anticipated to increase twelve to twenty-five times within the same period, illustrating the urgent need for targeted interventions [1]. In Europe and Central Asia, including Poland, rising rates of overweight and obesity exert growing pressure on healthcare systems, translating into significant direct and indirect costs such as hospitalizations, absenteeism, and reduced productivity [1, 2].

For women, the consequences of obesity extend beyond increased body weight to complex hormonal disturbances affecting reproductive, metabolic, and psychological health. These hormonal changes include disruptions in insulin regulation, estrogen and androgen balance, and alterations in leptin and ghrelin levels [1, 2]. These imbalances contribute to heightened risks of polycystic ovary syndrome (PCOS), insulin resistance, infertility, and cardiometabolic diseases [2]. Furthermore, high BMI has been linked to a substantial share of global disability-adjusted life years (DALYs) and premature mortality, exacerbating the burden on healthcare systems [1, 2].

Efforts to mitigate the impact of obesity require a multifaceted approach, addressing both systemic and individual factors. Strategies include promoting healthy lifestyles, nutrition education, and tailored weight management programs. Policymakers must prioritize investments in prevention and treatment to reduce the growing prevalence of obesity and its associated health and economic costs [1, 2].

This article aims to review the literature on the hormonal changes associated with obesity in women and the potential health consequences of these disturbances. By synthesizing global data and analyses, the study seeks to contribute to the understanding and management of this critical public health issue.

Analisis of the literature

Hormonal Dysregulation in Obese Women

Obesity is a global health challenge that significantly disrupts the body's hormonal function, particularly in women. Hormones play a central role in regulating metabolism, fertility, stress response and thyroid function

Obesity is not just excessive fat accumulation - it is a chronic low-grade inflammatory condition that affects the functioning of almost all endocrine systems. Adipokines such as leptin, adiponectin and resistin, secreted by adipose tissue, modulate the body's inflammatory response and affect glucose and lipid metabolism. Excessive adipose tissue is associated with increased secretion of pro-inflammatory cytokines (e.g. TNF- α , IL-6), which interfere with insulin action and affect the hypothalamic-pituitary-adrenal (HPA) axis [3, 4].

Adipose tissue is an active endocrine organ, producing estrogens through androgen aromatization. Excess estrogen, especially in premenopausal women, can lead to hyperestrogenism, resulting in irregular menstrual cycles, lack of ovulation and increased risk of endometrial cancer. During menopause, obesity exacerbates symptoms associated with estrogen deficiency, contributing to greater accumulation of visceral fat [5, 6].

In addition, obesity contributes to an increased risk of polycystic ovary syndrome (PCOS), a disorder characterized by hyperandrogenism, insulin resistance and ovulatory disorders. Coexisting with PCOS, insulin resistance and hyperinsulinemia exacerbate androgen production in the ovaries, creating a vicious cycle of metabolic and endocrine disorders [3, 7].

The aforementioned insulin resistance is a major component of metabolic disorders in obese women. Coexisting hyperinsulinemia, which further stimulates androgen production in the ovaries and reduces tissue sensitivity to insulin, contributes to the risk of type 2 diabetes. In addition, obesity affects the gut microbiome, which can modify glucose metabolism and increase inflammation in the body [8].

Adipokines are another group of hormones affected by excessively dilated adipose tissue. Adiponectin, a hormone that increases insulin sensitivity, is significantly reduced in

obese individuals. This is in contrast to leptin, the satiety hormone, which is secreted in excess, leading secondarily to leptin resistance. Dysfunction in the balance between adiponectin and leptin causes appetite dysregulation, which contributes to further weight gain and the progression of metabolic disorders [4, 7].

Obesity also increases the activity of the hypothalamic-pituitary-adrenal (HPA) axis, leading to chronically elevated levels of cortisol, also known as the stress hormone. Cortisol stimulates visceral fat deposition and increases insulin resistance. The coexistence of psychological stress in women with obesity exacerbates metabolic and endocrine disorders [3, 4].

Obese women are more likely to have subclinical hypothyroidism, which is associated with decreased basal metabolism and further weight gain. The association between obesity and autoimmune thyroid diseases such as Hashimoto's suggests the need to monitor thyroid antibody levels in overweight individuals [9, 10].

The gut microbiome also plays a key role in hormonal regulation, affecting glucose metabolism, thyroid function and stress response, among other factors. Obesity-related intestinal dysbiosis alters the production of short-chain fatty acids (SCFAs) and modulates the function of the HPA axis, which can exacerbate endocrine disruption. For this reason, probiotic and prebiotic interventions may be an important part of obesity treatment [5, 8].

Obesity affects hormones in a multidimensional way, creating a vicious cycle of metabolic, endocrine and inflammatory disorders. A key challenge is to develop individualized therapeutic strategies that address the unique interactions between hormones, diet, lifestyle and the gut microbiome. Interventions should include both pharmacotherapy and behavioral changes, such as dietary modification and regular physical activity.

Impact on Reproductive Health

Obesity is a significant risk factor for infertility in women. Infertility, defined as the inability to conceive after 12 months of regular, unprotected intercourse 3-4 times a week, affects an increasing number of women of reproductive age [11, 12]. In the United States, it is estimated that 15.5% of women in this age group experience infertility [11]. Studies have shown

that a high body mass index (BMI) is associated with irregular menstrual cycles, anovulation, and a longer time to conception. These issues are particularly pronounced in cases of abdominal obesity, which creates a detrimental hormonal and inflammatory environment, further disrupting reproductive physiology [13, 14, 15].

The mechanisms through which obesity leads to infertility are diverse and include hormonal dysregulation, reduced oocyte quality, impaired endometrial receptivity, and decreased efficacy of assisted reproductive technologies (ART) [16].

Obesity disrupts the functioning of the hypothalamic-pituitary-ovarian (HPO) axis, affecting the secretion of gonadotropin-releasing hormone (GnRH) and the levels of hormones such as luteinizing hormone (LH) and follicle-stimulating hormone (FSH) [13, 15, 17]. Excess adipose tissue also stimulates insulin production, which in turn leads to increased androgen synthesis in the ovaries. This overproduction of androgens is particularly evident in women with polycystic ovary syndrome (PCOS), exacerbating ovulatory disorders and reducing the chances of conception [15, 18, 19]. Additionally, adipokines such as leptin and adiponectin modulate reproductive functions. Leptin resistance disrupts hypothalamic signaling, while low adiponectin levels impair ovarian function and endometrial receptivity [13, 19].

Obese women often exhibit lower oocyte quality, resulting from abnormalities in meiotic division and mitochondrial damage [15, 17]. These processes are further aggravated by oxidative stress and chronic inflammation, which are hallmarks of obesity [15, 19]. Changes in follicular fluid, such as elevated levels of free fatty acids and triglycerides and reduced antioxidant potential, negatively affect embryo development, leading to lower fertilization and implantation rates [14, 16, 17, 20].

Obesity also significantly impacts endometrial receptivity. Studies have shown that obese women experience impaired decidualization and altered gene expression in the endometrium, which reduces the ability to accept an embryo [14, 17]. Dysregulated lipid metabolism in the endometrium further diminishes its capacity to support early embryo development, increasing the risk of implantation failures and miscarriages [15, 17].

Impact on Assisted Reproductive Technologies (ART)

Obesity significantly reduces the effectiveness of ART, such as in vitro fertilization (IVF). Obese women require higher doses of gonadotropins and longer ovarian stimulation cycles compared to women with normal body weight, resulting in fewer retrieved oocytes and lower fertilization and implantation rates [15, 19]. Live birth rates are also significantly lower in these women compared to those with a healthy weight [15].

The most effective approach to improving fertility in obese women is weight reduction through a healthy diet and regular physical activity. Even modest weight loss (5–10%) can restore menstrual regularity, increase ovulation frequency, and improve infertility treatment outcomes [11, 12, 21]. Pharmacotherapy, such as metformin, is particularly effective for women with PCOS, helping to regulate insulin and androgen levels [14, 19]. Bariatric surgeries, such as gastric bypass, lead to significant weight loss and improved reproductive function but are associated with risks of complications and require careful monitoring of nutritional status [12].

Obesity and polycystic ovary syndrome (PCOS)

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders affecting women of reproductive age, with a prevalence estimated at approximately 10–20% of this population. This condition significantly impacts reproductive health and is also associated with serious metabolic disturbances. Obesity, as an increasingly prevalent health issue, plays a key role in exacerbating PCOS symptoms and significantly complicates its treatment.

Obesity contributes to the development of PCOS through a series of complex mechanisms that affect hormonal and metabolic functions in women. One of the primary processes is insulin resistance, which occurs in about 75% of women with PCOS. In the case of obesity, this condition is further exacerbated because excess adipose tissue, particularly visceral fat, leads to elevated insulin levels in the blood. Hyperinsulinemia stimulates androgen production in ovarian thecal cells and adrenal glands, intensifying hyperandrogenism symptoms such as acne, hirsutism, and irregular menstruation [16, 22].

Additionally, insulin reduces the levels of sex hormone-binding globulin (SHBG), increasing the amount of free androgens and further disrupting ovarian function. Another significant mechanism is the low-grade chronic inflammation characteristic of both obesity and PCOS. Pro-inflammatory cytokines, such as IL-6 and TNF- α , impair insulin signaling and exacerbate oxidative stress, negatively impacting follicular maturation and ovulation [20, 22].

The presence of obesity in women with PCOS affects many aspects of their hormonal and metabolic health. One of the most significant issues is ovarian dysfunction, which results in halted follicular development and anovulation. Elevated androgen levels and changes in gonadotropin-releasing hormone (GnRH) pulsatility lead to an imbalance between luteinizing hormone (LH) and follicle-stimulating hormone (FSH), contributing to irregular menstrual cycles, anovulatory cycles, and other symptoms related to luteal phase dysfunction [16, 22, 23].

At the metabolic level, insulin resistance and glucose metabolism disturbances increase the risk of prediabetes and type 2 diabetes. Combined with dyslipidemia, characterized by elevated triglycerides and reduced HDL levels, women with PCOS and obesity face a heightened risk of developing cardiovascular diseases [20, 23].

Reproductive problems are also a significant aspect of PCOS. Obesity further prolongs the time required to conceive and increases the risk of pregnancy complications, such as gestational diabetes, preeclampsia, and miscarriage [16, 23].

Lifestyle modifications are crucial in treating PCOS associated with obesity. Weight loss, even by 5–10%, significantly improves insulin sensitivity, reduces androgen levels, and restores ovulation. A healthy diet, particularly one with a low glycemic load, and regular physical activity can markedly improve clinical outcomes [20, 23]. However, maintaining long-term weight loss is challenging, especially for women with PCOS, who may experience difficulties mobilizing fat and have reduced brown adipose tissue activity [16, 20].

Pharmacotherapy is another treatment component. Metformin improves insulin sensitivity and reduces hyperandrogenism, though its effects on weight reduction are limited. Promising results have been observed with drugs used for diabetes treatment, such as GLP-1 receptor agonists, which support weight loss, improve insulin sensitivity, and lower androgen levels. Combining these drugs with metformin yields particularly good outcomes, although further studies on long-term safety are needed [20, 24].

For women with severe obesity, bariatric surgery can be an effective option, leading to significant weight loss and improvements in metabolic and reproductive parameters. However, this method carries risks of complications, such as nutritional deficiencies and postoperative issues [23].

For these reasons, treatment should be holistic and tailored to the individual needs of patients, encompassing both lifestyle modifications and pharmacotherapy. Psychological support, particularly in addressing body image issues and low motivation, is crucial for treatment success [20, 24].

Early screening for metabolic disorders and further research on the long-term efficacy of new therapies, such as GLP-1 receptor agonists, are essential to improving treatment outcomes for women with PCOS and obesity. Through a comprehensive approach, it is possible not only to alleviate symptoms but also to improve the quality of life and reproductive potential of patients.

Obesity and Pregnancy Complications

Obesity is a global health issue that significantly impacts the health of pregnant women. Pregnant women with obesity face a substantially higher risk of complications such as hormonal disorders, gestational diabetes mellitus (GDM), and hypertension [16]. These complications result from complex interactions between metabolic, inflammatory, and hormonal processes.

During pregnancy, a woman's body undergoes significant hormonal adaptations to support fetal development. However, obesity disrupts these processes, leading to adverse outcomes for both the mother and the child. Obesity exacerbates the insulin resistance naturally present during pregnancy, resulting in hyperinsulinemia. Elevated insulin levels can overactivate signaling pathways, such as mTOR in the placenta, increasing nutrient transport to the fetus and causing macrosomia. These processes increase the risk of long-term metabolic disorders in the child [25]. Moreover, in pregnant women with obesity, adipokines play a crucial role in energy regulation and placental function. Elevated leptin levels promote placental inflammation and dysfunction, while significantly reduced adiponectin levels, which have anti-inflammatory properties and enhance insulin sensitivity, exacerbate metabolic dysfunctions and contribute to excessive fetal growth [26].

In pregnancies complicated by obesity, the placenta becomes less efficient at regulating nutrient transport, exposing the fetus to excessive glucose and lipids. These disruptions contribute to oxidative stress, inflammation, and lipid accumulation in the placenta, further impairing its function [25].

Obesity significantly increases the risk of gestational diabetes, characterized by glucose metabolism disturbances. The main mechanisms include exacerbated insulin resistance leading to inadequate glucose uptake by tissues, maternal hyperglycemia, fetal hyperinsulinemia, and excessive nutrient transfer, resulting in macrosomia and neonatal hypoglycemia after birth [25]. Additionally, this condition can have long-term health effects, such as an increased risk of obesity, type 2 diabetes, and metabolic syndrome in children born to mothers with GDM [26].

Another issue for pregnant women with obesity is a predisposition to hypertensive disorders, such as gestational hypertension and preeclampsia. Chronic inflammation, associated with elevated pro-inflammatory cytokines like TNF- α and IL-6, leads to endothelial dysfunction and increased vascular resistance [25]. Furthermore, lipid metabolism disturbances in obese women intensify oxidative stress and impair placental function, which is crucial for proper fetal development [26]. Another mechanism contributing to hypertension in pregnancy is placental hypoxia caused by blood flow abnormalities and improper vessel development, leading to maternal hypertension and an increased risk of preterm birth [25].

Lifestyle modifications, particularly adopting healthy dietary habits and regular physical activity before and during pregnancy, improve metabolism, reduce excessive weight gain, and lower the risk of GDM, hypertension, and preeclampsia [25, 26]. Low-dose aspirin may reduce the risk of preeclampsia in women at high risk [26]. Pre-pregnancy weight reduction through supervised diet and physical activity is the most effective way to mitigate complications. In cases of severe obesity, bariatric surgery may be considered, although it requires careful planning and monitoring [26]. Research into targeted therapies that modulate placental signaling and reduce inflammation offers a promising future for managing pregnancies affected by obesity [25].

Obesity poses a significant challenge to reproductive health, disrupting hormonal adaptations during pregnancy and increasing the risk of GDM and hypertension. Proactive approaches, including pre-pregnancy interventions, lifestyle modifications, and advanced

pharmacological therapies, are essential to improving health outcomes. Further research should focus on better understanding the molecular mechanisms underlying these complications to develop precise and effective interventions. Managing obesity during pregnancy not only enhances maternal and child health but also reduces the risk of metabolic diseases in future generations.

Cardiometabolic Consequences of Hormonal Changes

Obesity has a significant impact on hormonal balance in women, leading to severe cardiometabolic consequences. These disturbances are associated with an increased risk of cardiovascular diseases, dyslipidemia, and metabolic syndrome.

Obesity is closely linked to a heightened risk of cardiovascular diseases, such as venous thromboembolism, atherosclerosis, and ischemic heart disease. Hormonal changes, particularly in leptin and adiponectin levels, play a key role in these complications. Women with obesity often exhibit elevated leptin levels, leading to hyperleptinemia. Excess leptin contributes to vascular dysfunction and increased inflammation by activating oxidative stress and inflammatory pathways, resulting in endothelial damage and arterial stiffness. These processes are directly associated with a higher risk of vascular events such as heart attacks and strokes [27].

Conversely, adiponectin levels, which have anti-inflammatory and vascular-protective properties, are significantly reduced in women with obesity. A deficiency in adiponectin exacerbates oxidative stress and chronic inflammation, increasing the risk of atherosclerosis. The imbalance in the leptin-to-adiponectin ratio, characteristic of obesity, is considered a biomarker of cardiovascular risk and highlights the need for therapies that restore this balance [27, 4].

Dyslipidemia is one of the most common metabolic complications of obesity, characterized by elevated triglyceride levels and reduced high-density lipoprotein (HDL) cholesterol levels. These disturbances result from increased triglyceride production and impaired lipoprotein clearance, which are directly linked to insulin resistance and hormonal changes. Leptin resistance, typical of obesity, contributes to enhanced triglyceride synthesis in the liver, leading to hypertriglyceridemia. Simultaneously, low adiponectin levels adversely

affect reverse cholesterol transport, limiting HDL's ability to protect vessels from atherosclerosis. These lipid changes, exacerbated by inflammation and oxidative stress, promote the development of coronary artery disease and other cardiovascular complications [27, 4].

Androgens and insulin resistance play a central role in the pathogenesis of metabolic syndrome, which includes a range of disorders such as abdominal obesity, dyslipidemia, hypertension, and hyperglycemia. Hyperandrogenism, often observed in women with obesity, promotes visceral fat accumulation and exacerbates insulin resistance, further aggravating metabolic disorders. Women with PCOS, who frequently experience hyperandrogenism, have a significantly higher risk of developing metabolic syndrome [28]. Insulin resistance, a key mechanism leading to type 2 diabetes, disrupts glucose uptake in peripheral tissues and increases hepatic glucose production, resulting in hyperglycemia. At the same time, insulin resistance contributes to lipid disturbances by promoting triglyceride deposition in adipose tissue and other organs. Adipose tissue dysfunction, characterized by a low adiponectin-to-leptin ratio, reflects the interdependence between hormonal and metabolic disorders [27, 4].

To mitigate the cardiometabolic consequences of hormonal changes in women with obesity, a multifaceted approach is essential. Lifestyle interventions, such as weight reduction, regular physical activity, and a balanced diet, should form the cornerstone of treatment, as they improve adipokine profiles and insulin sensitivity. Pharmacotherapy aimed at correcting insulin resistance and hyperandrogenism should complement these efforts. Special attention should be given to therapies that modulate the adiponectin-to-leptin ratio and reduce inflammation. Improving cardiometabolic health in obese individuals requires early intervention and individualized therapy, tailored to the specific needs and risks of each patient. Research into more precise therapeutic strategies should be a priority to better manage the complex interactions between hormonal and metabolic disorders. Through a comprehensive approach, it is possible to significantly reduce the burden of cardiovascular diseases and metabolic syndrome in women with obesity.

Therapeutic Approaches

Obesity is one of the most significant health challenges of the modern world, particularly critical in the context of women's health, where excess body weight profoundly affects

hormonal balance, metabolic health, and reproductive capacity. Treating obesity requires an integrated approach that includes lifestyle modifications, pharmacological therapies, and surgical interventions. Each of these methods has unique benefits and limitations, which must be carefully considered to tailor treatment to the patient's needs.

Lifestyle modification is a fundamental and often the first step in treating obesity. Its main components include dietary changes, regular physical activity, and stress management. A proper diet and exercise regimen have a significant impact on hormonal functioning, which is especially important for women who often face hormonal imbalances such as insulin resistance or hyperandrogenism associated with polycystic ovary syndrome (PCOS). A diet based on a low glycemic load and appropriate calorie reduction helps with weight loss and improves insulin sensitivity, leading to better glucose metabolism and a reduced risk of type 2 diabetes. Regular physical activity, particularly when combined with diet, reduces visceral fat, improves metabolic balance, and supports reproductive health by restoring regular menstrual cycles and ovulation [20, 29].

Stress reduction is another critical aspect of lifestyle modification, as stress plays a key role in regulating cortisol levels. Chronic stress leads to elevated cortisol secretion, which promotes visceral fat accumulation and metabolic dysfunction. Relaxation techniques such as meditation, yoga, and cognitive-behavioral therapy effectively lower cortisol levels, supporting weight loss and hormonal balance [16].

While lifestyle modifications are effective and safe, they require long-term commitment and can be challenging to maintain, especially in environments that encourage unhealthy habits.

Pharmacotherapy is often used as a supplement to lifestyle changes, particularly for women with obesity who suffer from severe hormonal and metabolic imbalances. One of the most commonly used drugs is GLP-1 receptor agonists, such as liraglutide. These medications mimic incretin hormones, which regulate appetite, improve insulin sensitivity, and promote weight loss. Liraglutide not only supports weight reduction but also enhances reproductive health by lowering androgen levels and improving menstrual regularity in women with PCOS [20, 30].

Another pharmacological approach includes anti-androgen therapies, which reduce androgen levels in the body and help alleviate symptoms of hyperandrogenism, such as

hirsutism and acne. Drugs like spironolactone or flutamide are particularly effective, although they may cause side effects such as fatigue or electrolyte imbalances, limiting their long-term use [24].

Oral contraceptives are another option for treating hormonal disorders, such as PCOS. They help regulate menstrual cycles, reduce hyperandrogenism symptoms, and support reproductive health. However, in obese women, these medications may increase the risk of thromboembolic complications, so they should be used cautiously, with progestin-only preparations preferred in some cases [29].

Bariatric surgery is another treatment option. It is an effective method for managing severe obesity, particularly in cases where other treatments have not yielded satisfactory results. Procedures such as gastric bypass lead to significant and sustained weight loss, which is critical for improving hormonal and reproductive health. Post-surgery, patients experience substantial improvements in insulin sensitivity, increased adiponectin levels, and reduced hyperandrogenism, which contribute to better ovarian function, regular menstrual cycles, and enhanced fertility. Women who undergo bariatric surgery also face lower risks of pregnancy complications, such as gestational diabetes and preeclampsia [29, 31].

Despite its advantages, bariatric surgery carries risks such as nutritional deficiencies due to limited nutrient absorption. Patients require long-term vitamin and mineral supplementation and regular health monitoring to prevent potential complications [20].

Treating obesity in women requires a multifaceted approach combining lifestyle modifications, pharmacotherapy, and surgical interventions. Lifestyle changes should form the foundation of treatment, especially given their holistic and long-term health benefits. Pharmacotherapy is effective when rapid improvements in hormonal and metabolic functions are necessary but should be tailored to individual needs and monitored for potential side effects. Bariatric surgery, while effective, should be considered a last resort for severe obesity cases where other methods have failed. An integrated and personalized approach enables not only weight reduction but also improvements in hormonal health, metabolism, and overall quality of life for women struggling with obesity. Further research on the safety and efficacy of these therapies is essential to better adapt treatments to patients' needs.

Societal and Psychological Aspects

Obesity in women is not only a medical issue but also a phenomenon deeply rooted in societal norms, mental health, and systemic stigma. Social norms shaping body image, the psychological impact of hormonal disorders, and the stigma associated with access to healthcare are key aspects that require detailed analysis. Social norms greatly influence how women perceive their bodies and the impact on their mental health. Contemporary beauty standards, promoted by the media, often equate attractiveness with a slim figure, leading to widespread body dissatisfaction among women struggling with obesity. This dissatisfaction is reinforced by narratives that stigmatize larger body sizes and promote unattainable aesthetic ideals [32]. Such social pressure fosters the development of eating disorders, depression, and anxiety, especially in women who feel excluded due to their weight.

On the other hand, movements promoting body acceptance, such as the “body positivity” movement, seek to counteract these harmful narratives by emphasizing the value of diverse body shapes and encouraging self-acceptance. These initiatives have sparked important discussions about the consequences of weight stigma and the need for greater inclusivity. However, their impact is uneven, and many women continue to struggle with internalized shame driven by societal pressures [32].

Hormonal disorders associated with obesity, such as elevated cortisol levels, have a significant impact on women’s mental health, leading to depression and anxiety. Cortisol exacerbates these issues by disrupting the hypothalamic-pituitary-adrenal (HPA) axis. Dysregulation of this system worsens not only emotional but also physical problems, such as visceral fat accumulation and the development of metabolic syndrome [33].

Additionally, hormonal disorders like polycystic ovary syndrome (PCOS), which often co-occur with obesity, increase the risk of mental health problems. Hyperandrogenism and insulin resistance, characteristic of PCOS, are associated with heightened emotional stress, reduced self-esteem, and lower quality of life. Worse still, these psychological issues are often undiagnosed and insufficiently addressed in treatment, leaving many women without adequate support [33].

However, awareness and interest in the psychological consequences of hormonal disorders related to obesity are increasing. More therapeutic programs are combining psychological support with medical treatment, showing promising results in improving women's mental health [34].

Weight stigma significantly affects access to healthcare for women with obesity, especially in the areas of obesity treatment and reproductive health. Studies show that medical professionals often exhibit implicit biases against patients with obesity, leading to shorter consultations, less comprehensive care, and reluctance to address sensitive health topics like reproductive health. Women who experience stigma in healthcare settings are less likely to seek medical care, perpetuating a cycle of poor health outcomes [32].

Stigma extends beyond medical facilities, influencing public policy and societal attitudes toward obesity. Weight-related discrimination contributes to systemic barriers, such as limited access to subsidized obesity treatment and the perception of the condition as solely the result of individual neglect. These challenges disproportionately affect women, deepening health inequities and limiting their opportunities for health improvement [32, 33].

Addressing the societal and psychological challenges of obesity in women requires a multidimensional approach. First, educational campaigns should counter stereotypes about obesity by promoting a scientific understanding of its causes and consequences. Second, healthcare system reform is necessary, including training for medical staff to reduce bias and improve communication with patients with obesity. Psychological support should be an integral part of treatment, and health programs should combine medical therapy with emotional counseling. Finally, community-level initiatives, such as support groups and body acceptance campaigns, can help women cope with societal pressure and improve their mental health. While societal norms, hormonal disorders, and stigma create significant barriers, growing awareness and targeted interventions offer a real chance for positive change. Education, healthcare system reform, and integrating psychological support with medical treatment are key elements in improving the situation for women with obesity. Collaborative social and systemic efforts can significantly reduce the burden of stigma and improve health outcomes for this group.

Conclusion

The review highlights key hormonal disruptions, such as alterations in insulin regulation, adipokine levels, and reproductive hormone balance, which contribute to conditions like PCOS, infertility, and cardiometabolic diseases. Understanding these mechanisms is crucial for developing targeted therapeutic strategies and preventive measures. Future research should focus on personalized interventions, integrating lifestyle modifications, pharmacotherapy, and emerging clinical tools to mitigate the impact of obesity on women's health.

Disclosure

Author's contribution: KP

Conceptualization: KP, PS, WT

Methodology: KP

Software: PS, WT

Check: AS, WP

Formal analysis: WP, KP

Investigation: KP, AS

Resources: KP

Data curation: ML, WT, WM

Writing-rough preparation: PS, JK, ML

Writing-review and editing: KP, WT, PD

Visualization: KP, MG

Supervision: AN, JK

Project administration: KP

Supplementary Materials: They have not been provided.

Funding Statement: This research received no external funding.

References

- 1. Okunogbe A, Nugent R, Spencer G, Powis J, Ralston J, Wilding J. Economic impacts of overweight and obesity: current and future estimates for 161 countries.**

- BMJ Glob Health. 2022 Sep;7(9):e009773. doi: 10.1136/bmjgh-2022-009773. PMID: 36130777; PMCID: PMC9494015.
2. GBD 2019 Risk Factors Collaborators. Global burden of 87 risk factors in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet*. 2020 Oct 17;396(10258):1223-1249. doi: 10.1016/S0140-6736(20)30752-2. PMID: 33069327; PMCID: PMC7566194.
 3. Eng PC, Phylactou M, Qayum A, Woods C, Lee H, Aziz S, Moore B, Miras AD, Comninou AN, Tan T, Franks S, Dhillo WS, Abbara A. Obesity-Related Hypogonadism in Women. *Endocr Rev*. 2024 Mar 4;45(2):171-189. doi: 10.1210/endrev/bnad027. PMID: 37559411; PMCID: PMC10911953.
 4. Frühbeck G, Catalán V, Rodríguez A, Gómez-Ambrosi J. Adiponectin-leptin ratio: A promising index to estimate adipose tissue dysfunction. Relation with obesity-associated cardiometabolic risk. *Adipocyte*. 2018 Jan 2;7(1):57-62. doi: 10.1080/21623945.2017.1402151. Epub 2017 Dec 5. PMID: 29205099; PMCID: PMC5915018.
 5. Leeners B, Geary N, Tobler PN, Asarian L. Ovarian hormones and obesity. *Hum Reprod Update*. 2017 May 1;23(3):300-321. doi: 10.1093/humupd/dmw045. PMID: 28333235; PMCID: PMC5850121.
 6. Palacios S, Chedraui P, Sánchez-Borrego R, Coronado P, Nappi RE. Obesity and menopause. *Gynecol Endocrinol*. 2024 Dec;40(1):2312885. doi: 10.1080/09513590.2024.2312885. Epub 2024 Feb 11. PMID: 38343134.
 7. Castela I, Morais J, Barreiros-Mota I, Silvestre MP, Marques C, Rodrigues C, Ismael S, Araújo JR, Ângelo-Dias M, Martins C, Borrego LM, Monteiro R, Coutinho SR, Calhau C, Martins C, Faria A, Pestana D, Teixeira D. Decreased adiponectin/leptin ratio relates to insulin resistance in adults with obesity. *Am J Physiol Endocrinol Metab*. 2023 Feb 1;324(2):E115-E119. doi: 10.1152/ajpendo.00273.2022. Epub 2022 Nov 9. PMID: 36351292.
 8. Ludwig DS, Aronne LJ, Astrup A, de Cabo R, Cantley LC, Friedman MI, Heymsfield SB, Johnson JD, King JC, Krauss RM, Lieberman DE, Taubes G, Volek JS, Westman EC, Willett WC, Yancy WS, Ebbeling CB. The carbohydrate-insulin model: a physiological perspective on the obesity pandemic. *Am J Clin Nutr*. 2021 Dec 1;114(6):1873-1885. doi: 10.1093/ajcn/nqab270. PMID: 34515299; PMCID: PMC8634575.

9. Safari S, Rafrat M, Malekian M, Molani-Gol R, Asghari-Jafarabadi M, Mobasseri M. Effects of vitamin D supplementation on metabolic parameters, serum irisin and obesity values in women with subclinical hypothyroidism: a double-blind randomized controlled trial. *Front Endocrinol (Lausanne)*. 2023 Dec 21;14:1306470. doi: 10.3389/fendo.2023.1306470. PMID: 38179303; PMCID: PMC10764604.
10. Wang B, Song R, He W, Yao Q, Li Q, Jia X, Zhang JA. Sex Differences in the Associations of Obesity With Hypothyroidism and Thyroid Autoimmunity Among Chinese Adults. *Front Physiol*. 2018 Oct 4;9:1397. doi: 10.3389/fphys.2018.01397. PMID: 30337885; PMCID: PMC6180185.
11. Tang J, Xu Y, Wang Z, Ji X, Qiu Q, Mai Z, Huang J, Ouyang N, Chen H. Association between metabolic healthy obesity and female infertility: the national health and nutrition examination survey, 2013-2020. *BMC Public Health*. 2023 Aug 10;23(1):1524. doi: 10.1186/s12889-023-16397-x. PMID: 37563562; PMCID: PMC10416469.
12. Zain MM, Norman RJ. Impact of obesity on female fertility and fertility treatment. *Womens Health (Lond)*. 2008 Mar;4(2):183-94. doi: 10.2217/17455057.4.2.183. PMID: 19072520.
13. Silvestris E, de Pergola G, Rosania R, Loverro G. Obesity as disruptor of the female fertility. *Reprod Biol Endocrinol*. 2018 Mar 9;16(1):22. doi: 10.1186/s12958-018-0336-z. PMID: 29523133; PMCID: PMC5845358.
14. Practice Committee of the American Society for Reproductive Medicine. Obesity and reproduction: a committee opinion. *Fertil Steril*. 2015 Nov;104(5):1116-26. doi: 10.1016/j.fertnstert.2015.08.018. Epub 2015 Oct 1. PMID: 26434804.
15. Broughton DE, Moley KH. Obesity and female infertility: potential mediators of obesity's impact. *Fertil Steril*. 2017 Apr;107(4):840-847. doi: 10.1016/j.fertnstert.2017.01.017. Epub 2017 Mar 11. PMID: 28292619.
16. Cena H, Chiovato L, Nappi RE. Obesity, Polycystic Ovary Syndrome, and Infertility: A New Avenue for GLP-1 Receptor Agonists. *J Clin Endocrinol Metab*. 2020 Aug 1;105(8):e2695–709. doi: 10.1210/clinem/dgaa285. PMID: 32442310; PMCID: PMC7457958.
17. Yang T, Zhao J, Liu F, Li Y. Lipid metabolism and endometrial receptivity. *Hum Reprod Update*. 2022 Nov 2;28(6):858-889. doi: 10.1093/humupd/dmac026. PMID: 35639910.

18. Zheng L, Yang L, Guo Z, Yao N, Zhang S, Pu P. Obesity and its impact on female reproductive health: unraveling the connections. *Front Endocrinol (Lausanne)*. 2024 Jan 9;14:1326546. doi: 10.3389/fendo.2023.1326546. PMID: 38264286; PMCID: PMC10803652.
19. Ferrell EL, Choudhry AA, Schon SB. Obesity and In Vitro Fertilization. *Semin Reprod Med*. 2023 Jul;41(3-04):87-96. doi: 10.1055/s-0043-1776420. Epub 2023 Nov 1. PMID: 37913788.
20. Bednarz K, Kowalczyk K, Cwynar M, Czapla D, Czarkowski W, Kmita D, Nowak A, Madej P. The Role of Glp-1 Receptor Agonists in Insulin Resistance with Concomitant Obesity Treatment in Polycystic Ovary Syndrome. *Int J Mol Sci*. 2022 Apr 14;23(8):4334. doi: 10.3390/ijms23084334. PMID: 35457152; PMCID: PMC9029608.
21. Sustarsic A, Hadzic V, Meulenberg CJW, Abazovic E, Videmsek M, Burnik Papler T, Paravlic AH. The influence of lifestyle interventions and overweight on infertility: a systematic review, meta-analysis, and meta-regression of randomized controlled trials. *Front Med (Lausanne)*. 2023 Nov 1;10:1264947. doi: 10.3389/fmed.2023.1264947. PMID: 38020109; PMCID: PMC10646477.
22. Wang J, Yin T, Liu S. Dysregulation of immune response in PCOS organ system. *Front Immunol*. 2023 May 5;14:1169232. doi: 10.3389/fimmu.2023.1169232. PMID: 37215125; PMCID: PMC10196194.
23. Marinelli S, Napoletano G, Straccamore M, Basile G. Female obesity and infertility: outcomes and regulatory guidance. *Acta Biomed*. 2022 Aug 31;93(4):e2022278. doi: 10.23750/abm.v93i4.13466. PMID: 36043953; PMCID: PMC9534231.
24. Bader S, Bhatti R, Mussa B, Abusanana S. A systematic review of GLP-1 on anthropometrics, metabolic and endocrine parameters in patients with PCOS. *Womens Health (Lond)*. 2024 Jan-Dec;20:17455057241234530. doi: 10.1177/17455057241234530. PMID: 38444070; PMCID: PMC10916466.
25. Kelly AC, Powell TL, Jansson T. Placental function in maternal obesity. *Clin Sci (Lond)*. 2020 Apr 30;134(8):961-984. doi: 10.1042/CS20190266. PMID: 32313958; PMCID: PMC8820171.
26. Strauss A. Obesity in pregnant women: maternal, fetal, and transgenerational consequences. *Eur J Clin Nutr*. 2021 Dec;75(12):1681-1683. doi: 10.1038/s41430-021-01015-z. Epub 2021 Oct 26. PMID: 34702963; PMCID: PMC8636246.

27. Zhao S, Kusminski CM, Scherer PE. Adiponectin, Leptin and Cardiovascular Disorders. *Circ Res.* 2021 Jan 8;128(1):136-149. doi: 10.1161/CIRCRESAHA.120.314458. Epub 2021 Jan 7. PMID: 33411633; PMCID: PMC7799441.
28. Rosano GMC, Rodriguez-Martinez MA, Spoletini I, Regidor PA. Obesity and contraceptive use: impact on cardiovascular risk. *ESC Heart Fail.* 2022 Dec;9(6):3761-3767. doi: 10.1002/ehf2.14104. Epub 2022 Sep 14. Erratum in: *ESC Heart Fail.* 2023 Apr;10(2):1497. doi: 10.1002/ehf2.14322. PMID: 36103980; PMCID: PMC9773763.
29. Muscogiuri G, Verde L, Vetrani C, Barrea L, Savastano S, Colao A. Obesity: a gender-view. *J Endocrinol Invest.* 2024 Feb;47(2):299-306. doi: 10.1007/s40618-023-02196-z. Epub 2023 Sep 23. PMID: 37740888; PMCID: PMC10859324.
30. Elkind-Hirsch KE, Chappell N, Shaler D, Storment J, Bellanger D. Liraglutide 3 mg on weight, body composition, and hormonal and metabolic parameters in women with obesity and polycystic ovary syndrome: a randomized placebo-controlled-phase 3 study. *Fertil Steril.* 2022 Aug;118(2):371-381. doi: 10.1016/j.fertnstert.2022.04.027. Epub 2022 Jun 13. PMID: 35710599.
31. Locatelli JC, Costa JG, Haynes A, Naylor LH, Fegan PG, Yeap BB, Green DJ. Incretin-Based Weight Loss Pharmacotherapy: Can Resistance Exercise Optimize Changes in Body Composition? *Diabetes Care.* 2024 Oct 1;47(10):1718-1730. doi: 10.2337/dci23-0100. PMID: 38687506.
32. Stanford FC, Tauqeer Z, Kyle TK. Media and Its Influence on Obesity. *Curr Obes Rep.* 2018 Jun;7(2):186-192. doi: 10.1007/s13679-018-0304-0. PMID: 29637412; PMCID: PMC5959781.
33. van der Valk ES, Savas M, van Rossum EFC. Stress and Obesity: Are There More Susceptible Individuals? *Curr Obes Rep.* 2018 Jun;7(2):193-203. doi: 10.1007/s13679-018-0306-y. PMID: 29663153; PMCID: PMC5958156.
34. Guglielmi V, Dalle Grave R, Leonetti F, Solini A. Female obesity: clinical and psychological assessment toward the best treatment. *Front Endocrinol (Lausanne).* 2024 May 3;15:1349794. doi: 10.3389/fendo.2024.1349794. PMID: 38765954; PMCID: PMC11099266.