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Obesity and reproductive health: Pathophysiological mechanisms and emerging interventions

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Abstract

This review examines the multifaceted relationship between obesity and human reproduction, emphasizing the molecular, cellular, and systemic mechanisms by which excessive adiposity impairs fertility in both women and men. We synthesized findings from epidemiological, experimental, and clinical studies to explore how obesity influences hormonal balance, gametogenesis, and treatment outcomes in assisted reproduction. Mechanistic pathways, including insulin resistance, mitochondrial dysfunction, oxidative and endoplasmic reticulum stress, were critically analyzed. In women, obesity disrupts ovulation, oocyte maturation, and hormonal regulation, primarily through insulin resistance, altered adipokine secretion, and mitochondrial and ER stress. In men, obesity compromises spermatogenesis, testosterone production, and sperm quality via hormonal imbalance, oxidative stress, and inflammation. These disruptions lead to poorer outcomes in fertility treatments, including decreased oocyte quality and live birth rates. However, interventions such as weight reduction, pharmacological therapies (metformin, GLP-1 agonists), and bariatric surgery significantly improve reproductive outcomes. Obesity exerts profound, bidirectional effects on reproductive health through metabolic and molecular disturbances. Comprehensive management integrating lifestyle, pharmacological, and surgical strategies offers a promising route to restore fertility in obese individuals. Recognizing obesity as a critical determinant of reproductive potential highlights the need for integrated metabolic and reproductive care.

Keywords: Adiposity, Endocrine dysfunction, Infertility, Inflammation, Metabolic interventions.

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1. Introduction

In today's world, the increasing rate of obesity has become a significant public health issue, affecting various aspects of human health. Obesity, characterized by an excessive buildup of fat, is no longer seen just as a result of lifestyle choices but has evolved into a complex condition with deep impacts on bodily and metabolic functions. The World Health Organization reported that in 2011, over 1.6 billion adults were overweight, and 400 million were obese, underlining the gravity of this issue on a global scale [1, 2].

Along with the growing problem of obesity, female infertility, which is the inability to achieve a clinical pregnancy after 12 months of regular unprotected sex, is also rising as a critical global health concern. The delicate balance of hormones, cell functions, and body structures essential for female fertility can be easily disrupted, and obesity, with its broad systemic effects, has been pinpointed as a major factor. The overlap of these two health issues presents a complicated scenario [3, 4]. Obesity can directly affect women's reproductive health through its metabolic and hormonal changes. Conversely, the psychological effects of infertility can lead to behaviors that promote weight gain, forming a difficult cycle to break. Recognizing this connection is crucial for several reasons. It has immediate health consequences for those involved and wider social and economic impacts. Infertility can cause deep psychological pain, affecting personal relationships, mental health, and life quality. Additionally, in many societies, the ability to have children is closely tied to cultural roles and expectations, leading to stigma and exclusion for those who are infertile [5, 6].

Moreover, the financial costs of treating infertility, especially when linked with obesity, are significant. From testing to treatment, the expenses can be overwhelming, putting more pressure on healthcare systems that are already under strain. In this review, we aim to explore the complex ways obesity affects female reproductive health. By examining a wide range of epidemiological, clinical, and molecular research, we strive to offer a thorough understanding of this important intersection between metabolic and reproductive health [7, 8].

2. Ovulation and Menstrual Cycle Abnormalities

As early as 1633, the French surgeon and obstetrician Paré noted cases of women with increased weight, absence of menstruation, and signs of elevated male hormones. In the seminal account of Stein–Leventhal syndrome, obesity was observed in three out of seven patients with rare or absent menstrual cycles. The first detailed study exploring the link between obesity and menstrual irregularities found a 48% obesity rate among 60 women without menstruation, compared to a 13% rate in a group with regular menstrual cycles [9, 10]. Generally, studies indicate that 30%-36% of obese women experience menstrual irregularities, though reports vary widely from under 10% to over 50%. In a study comparing 597 women with anovulatory primary infertility to 1,695 women with at least one child, the relative risks of infertility due to lack of ovulation were significantly higher: 3.1 (95% confidence interval [CI], 2.2–4.4) and 2.4 (95% CI, 1.7–3.3) for those with a body mass index (BMI) over 27 kg/m^2, both before and after adjusting for age and physical activity [11, 12]. The likelihood of experiencing absent or infrequent menstruation climbs with increasing levels of overweight or obesity, both in adults and adolescents. Being obese at age 7 is a standalone risk factor for menstrual issues by age 33 [13, 14].

Women with obesity are more prone to ovulatory dysfunction, often complicated by the presence of polycystic ovary syndrome (PCOS). According to the Nurses' Health Study, the risk of infertility due to lack of ovulation escalates with increasing BMI. Higher BMI at age 18 was also linked to a greater risk of anovulatory infertility, regardless of PCOS diagnosis (relative risk [RR], 1.0, and BMI, 20.0–21.9; 1.3 and BMI, 24–25.9; 1.7 and BMI, 26–27.9; 2.4 and BMI, 28–29.9; 2.7 and BMI, 30–31.9; and 2.7 and BMI, >32 kg/m2) [15, 16]. The distribution of body fat plays a crucial role, as women with ovulatory dysfunction tend to have a larger waist circumference and more abdominal fat compared to ovulatory women of similar BMI. Further research supports that abdominal fat is a stronger predictor of ovulatory dysfunction than overall body fat [17, 18].

Obesity is frequently observed in individuals with PCOS, making PCOS a complicating factor in understanding these relationships. The impact of BMI on the likelihood of ovulatory issues, especially when PCOS is not a factor, remains unclear. This is partly due to the diverse criteria and manifestations of PCOS. While obesity rates in women with PCOS have risen, mirroring the general population's increase, the risk of developing PCOS due to obesity is relatively small [19, 20].

Modest weight reduction, achieved through lifestyle changes with or without the help of weight loss drugs, has shown to improve ovulation and regulate menstrual cycles in women with PCOS. Furthermore, bariatric surgery has led to the resolution of amenorrhea in many obese women. However, accurately assessing the prevalence or risk of menstrual irregularities in obese women is difficult [6, 21]. This difficulty is compounded by the reliance on retrospective self-reports for most studies on menstrual irregularities, the accuracy of which has been questioned, especially in women with atypical average menstrual cycle lengths [22, 23].

Differences in reproductive hormones are observed among women across different BMI categories, even when they have regular menstrual cycles, indicating that the impact of obesity on menstrual function varies in severity. In obese women with ovulatory cycles, there are notable changes including reduced levels of luteinizing hormone (LH) throughout the cycle, diminished LH pulse amplitude during the early follicular phase, decreased levels of follicle-stimulating hormone throughout the cycle, prolonged follicular phases, shortened luteal phases, and lower levels of luteal phase progesterone metabolites compared to women of normal weight with ovulatory cycles [24, 25].

Central obesity and an increase in visceral fat can lead to insulin resistance and elevated insulin levels. This insulin resistance can further lead to increased levels of androgens due to its direct effect on the ovaries and by reducing the production of sex hormone-binding globulin in the liver, which is often associated with PCOS [26]. The presence of high androgen levels, along with increased conversion of androgens to estrogens in fat tissue, the accumulation of sex steroids in

adipose tissue, changes in leptin and other adipokine levels, alterations in insulin-like growth factor binding protein production, and compromised function of granulosa cells, all disrupt the normal functioning of the hypothalamic–pituitary–gonadal axis, leading to menstrual irregularities [27, 28].

3. Effects of Obesity on the Oocyte Maturation

In bisexual reproduction, the female gametes are primarily responsible for storing energy and matter crucial for the development of the zygote later on. The process of developing female gametes is intricate and highly specialized. In higher animals, particularly mammals, follicles serve as the foundational structure for the development of female gametes. The development of follicles involves two main processes: firstly, the germ cell undergoes an orderly suspension and resumption of development, achieving maturation in both the nucleus and cytoplasm of the oocyte [29, 30]. Secondly, follicular cells experience various stages of differentiation and proliferation, regulating the orderly development of germ cells while also fulfilling their hormonal functions. A key aspect of the initial stage of follicular development is the growth of oocytes, which is crucial for determining the potential of the embryo. Oocytes within primordial follicles are halted in the prophase of meiosis I, becoming primary oocytes. As oocytes grow to a certain size, they acquire the capability to resume meiosis. At this stage, oocytes possess large nuclei, loosely packed chromatin, and intact nuclear membranes, known as germinal vesicles (GV) [31, 32]. If fully grown oocytes are released from follicular restraint, they may spontaneously resume meiosis, a process referred to as germinal vesicle breakdown (GVBD). Following GVBD, oocytes complete the first meiotic division, separate homologous chromosomes, and expel the first polar body. Subsequently, spindles reassemble, and oocytes proceed to metaphase II, remaining in this stage until fertilization occurs. However, studies have shown that oocytes collected from both obese women and mice are of inferior quality, suggesting that obesity adversely affects oocyte maturation [33-35].

3.1. Meiotic Maturation

Full meiotic maturation involves the continuation of meiosis and accurate chromosome segregation. An oocyte in meiotic arrest is identified by its nucleus, which possesses GV. The commencement of meiotic resumption is marked by the GVBD. Following GVBD, the oocyte completes the first meiotic division, segregates homologous chromosomes, and ejects the first polar body [34, 36]. The spindle then reorganizes and progresses to the second meiotic metaphase until fertilization occurs. In mouse models of obesity induced by a high-fat diet, 39.45% of oocytes from obese mice achieved GVBD, in contrast to 89.46% of oocytes from the control group, and oocytes from obese mice were also smaller than those from controls. Additionally, oocyte maturation in obese mice during in vitro fertilization (IVF) was observed to be delayed [37, 38].

The spindle, essential for chromosome separation, is a dynamic structure primarily made up of longitudinally aligned microtubules. Its function is to gather, sort, and distribute chromosomes to the daughter cells during division. During the first meiotic division, GVBD triggers the formation of bipolar spindles around chromosomes. At the conclusion of this stage, the spindle moves to the cortex, initiating cortical reorganization. Following the extrusion of the first polar body, oocytes enter the second meiotic division, and spindles form rapidly beneath the first polar body [39]. The spindle's integrity is crucial for accurate chromosome segregation, and any segregation errors can result in aneuploidy, leading to early pregnancy loss. Polarized light microscopy can identify spindle abnormalities in oocytes, and the likelihood of encountering oocytes with disorganized spindles and misaligned chromosomes was significantly higher in severely obese groups compared to normal BMI groups [40]. Research in high-fat diet (HFD)-induced obesity models aligns with clinical observations in humans, showing a notable increase in abnormal spindle structures and chromosome misalignment in oocytes from HFD mice. Moreover, analysis of oocytes from diet-induced obesity (DIO) mice showed a high incidence of meiotic aneuploidy, characterized by disordered spindles and chromosomes not properly aligned on the metaphase plate [41, 42].

3.2. Mitochondrial Dysfunction

Oocyte maturation encompasses two distinct processes: the resumption of meiosis, known as nuclear maturation, and cytoplasmic maturation. The latter is crucial for determining the fertilization capacity of the mature oocyte and the developmental potential of the early embryo. A key player in this process is the mitochondria, the primary organelles inherited from the mother, located in the oocyte's cytoplasm. These organelles are pivotal for maturation, fertilization, and embryonic development, primarily through their role in generating 5'-adenosine triphosphate (ATP) via the tricarboxylic acid (TCA) cycle and oxidative phosphorylation (OXPHOS) [43, 44]. It is observed that mitochondrial DNA (mtDNA) copy numbers can increase more than 30-fold from primary oocytes to the MII stage oocytes. Oocytes with higher mtDNA copy numbers tend to be more robust and are more likely to be successfully fertilized than those with lower mtDNA numbers, indicating a correlation between mtDNA copy number and oocyte quality. During maturation, an increase in the mitochondrial membrane potential is noted, which boosts OXPHOS activity [45, 46]. This increase is critical for oocyte development, as a lack of membrane potential can diminish the oocyte's developmental potential. Additionally, higher ATP levels are associated with improved fertilization rates and embryo development [47, 48].

In the context of obesity, oocytes from obese mice display significantly higher mtDNA copy numbers compared to those from lean mice, alongside increased expression of mitochondrial biogenesis and fission markers (PGC-1α and Drp-1), and elevated levels of mtTFAM and NRF1, which are nuclear genes encoding mtDNA transcription factors. These changes suggest that oxidative stress from obesity leads to mitochondrial damage, triggering compensatory increases in mitochondrial biogenesis and fission [49, 50]. However, mitochondria in oocytes from obese mice show structural

abnormalities, such as fewer cristae, disorganized arrangement, reduced electron density, increased swelling, and vacuolation. Moreover, these mitochondria tend to clump together rather than being evenly distributed throughout the ooplasm, as seen in normal mice. Studies using potentiometric fluorescent dyes have shown that while some obese mice models exhibit increased membrane potential in oocytes and zygotes, generally, the mitochondrial membrane potential in oocytes from obese mice is lower than in those from lean mice [51, 52]. Additionally, oocytes from obese mice have been found to be more oxidized with a higher rate of reactive oxygen species (ROS) production. Collectively, these findings indicate that obesity negatively impacts mitochondrial structure, distribution, and function in oocytes, adversely affecting oocyte maturation [53, 54].

3.3. Endoplasmic Reticulum Stress

The endoplasmic reticulum (ER) is an essential cellular organelle involved in the synthesis, folding, trafficking of proteins, and the regulation of calcium levels. ER stress arises when the ER in liver and adipose tissues becomes overloaded with misfolded proteins. Research has shown that obesity can induce ER stress in mammalian cells. In obese pregnant women, markers of ER stress such as inositol requiring enzyme 1α (IRE1α), glucose-regulated protein 78 (GRP78), and X-box binding protein 1 (XBP1) were found to be significantly elevated in adipose tissue compared to their lean counterparts [55, 56]. Similarly, ER stress levels were higher in the adipose tissue of women with gestational diabetes mellitus than in those with normal glucose tolerance and comparable BMI. In the placenta, the expression of ER stress-related factors XBP1, activating transcription factor 4 (Atf4), and the molecular chaperone calnexin were reduced following a HFD during pregnancy [57, 58].

Protein synthesis, crucial for oocyte maturation, relies on the translation of maternal mRNA. The ER is vital in supporting the increased protein requirements of oocytes through accurate protein synthesis, folding, and modification, highlighting the importance of managing ER stress during oocyte maturation. Lipid accumulation occurs not only in adipose but also in non-adipose tissues, leading to elevated free fatty acid levels, lipotoxicity, and ER stress, which is linked to mitochondrial damage [59, 60]. Evidence of ER stress impacting oocyte quality includes studies where cumulus-oocyte complexes (COCs) exposed to thapsigargin, a potent ER stress inducer, showed reduced cumulus cell expansion and poor pre-implantation development. Similarly, exposure to palmitic acid, another ER stress inducer, diminished cumulus expansion and impaired pre-implantation development. Remarkably, treating COCs with the ER stress inhibitor salubrinal, either after exposure to an ER stress inducer or from obese mice, improved oocyte quality [61]. This improvement was indicated by increased levels of mitochondrial replication factors, such as mitochondrial transcription factor A (TFAM) and dynamin-related protein 1 (DRP1), along with mitochondrial DNA in the oocytes of obese mice. These findings underscore the critical role of ER stress in the interactions within cumulus-oocyte complexes and in maintaining oocyte quality [62].

4. Altered Ovarian Responsiveness and Oocyte Quality with Fertility Treatments

Besides experiencing higher instances of ovulatory issues, obesity is also linked to poorer results following infertility treatments. Research indicates that changes in follicle development and reduced egg quality may play a role in these outcomes [63, 64].

4.1. Responsiveness to Ovarian Stimulation

In women with normogonadotropic anovulation, higher BMI and abdominal obesity are linked to reduced chances of ovulating in response to clomiphene citrate treatment (for increased BMI, the odds ratio [OR] is 0.92 [0.88–0.96]; for increased waist-to-hip ratio, the OR is 0.60 [0.40–0.89]). A significant randomized study revealed that treatment with letrozole led to higher live birth rates (LBRs) compared to clomiphene citrate, especially in women with a higher BMI [65]. This suggests a different underlying mechanism or that clomiphene citrate might be underdosed in these cases. Moreover, obese women undergoing ovulation induction with gonadotropins need larger doses of these medications and yield fewer follicles for each dose used. Extensive retrospective studies involving 1,721 to 8,145 women receiving assisted reproductive technologies (ARTs) have also shown that obesity negatively affects the ovaries' response to gonadotropin stimulation, indicated by longer treatment durations, higher amounts of gonadotropins needed, more frequent cycle cancellations, and fewer oocytes collected [66, 67].

4.2. Oocyte Quality

Numerous studies have explored the link between obesity and the quality of oocytes and the embryos that result. Women with obesity who undergo IVF experience changes in the follicular environment, including increased insulin levels, inflammation markers, and higher free fatty acid levels, which are associated with abnormalities in cumulus-oocyte complexes. Oocytes from overweight or obese women are typically smaller compared to those from women of normal weight. The relationship between fertilization rates and maternal BMI has shown mixed results [68, 69]. While obesity seems to affect the blastulation rates and metabolism of developing embryos, the rate of euploid embryos remains consistent across different BMI categories. In 2016, two extensive retrospective analyses using data from the Centers for Disease Control and Prevention's National ART Surveillance System and the SART Clinic Outcome Reporting System database examined how BMI impacts IVF outcomes. Both studies found a decline in pregnancy rates and LBR with higher BMI [70, 71]. However, the decline in fertility due to age has a more significant effect on LBR at older ages, indicating that delaying IVF to lose weight may not be beneficial for older women who are overweight or obese. Moreover, ovulation induction in women with PCOS shows decreased LBRs as BMI increases [72].

These findings are supported by studies using obese mouse models induced by diet, where obesity was found to compromise oocyte quality through mitochondrial dysfunction, increased levels of reactive oxygen species, and issues with meiotic spindles and chromosomal alignment. Notably, in mouse models, interventions like weight loss, increased physical activity, and antioxidant treatments have not been successful in reversing the adverse effects on oocyte quality caused by diet-induced obesity [73].

In summary, a higher BMI is linked to reduced ovarian response to ovulation induction, necessitating higher doses of medication and resulting in fewer oocytes retrieved during IVF. Both animal models and human clinical studies demonstrate that oocyte quality is compromised by obesity. There is a direct correlation between higher BMI and lower rates of implantation, clinical pregnancy, and LBRs in IVF/intracytoplasmic sperm injection treatments. This impact is most pronounced in younger women of reproductive age and diminishes as reproductive age advances [74, 75].

5. The Relationship Between Obesity and Male Reproduction

Nutrition plays a crucial role in affecting fertility, with numerous studies highlighting the negative impact of obesity on male fertility. Research indicates that obese men have a significantly higher chance of experiencing infertility compared to men of normal weight (OR = 1.66, 95% CI 1.53–1.79). Additionally, obesity in men is linked to lower success rates in ART, including a notable decrease in pregnancy (OR 0.78, 95% CI 0.63 to 0.98, p = 0.03) and live birth (OR 0.88, 95% CI 0.82 to 0.95, p = 0.001) rates in cycles of intracytoplasmic sperm injection (ICSI) [76-78].

Obesity can harm the male reproductive system by affecting erectile function and reducing semen quality. Evidence shows a negative correlation between BMI and sperm concentration, motility, and normal morphology. Reviews and meta-analyses have found that obesity and overweight conditions are associated with a greater prevalence of azoospermia (no sperm cells) and oligozoospermia (few sperm cells), increased sperm DNA fragmentation, abnormal sperm chromatin compactness, a higher percentage of sperm with low mitochondrial membrane potential, and phosphatidylserine externalization, which is an early sign of apoptosis (programmed cell death) [79-81].

The damage to sperm caused by obesity is believed to result from several factors, including disrupted reproductive hormone levels, insulin resistance, altered adipokine production, higher scrotal temperature, increased oxidative stress, and chronic inflammation. Excessive visceral fat reduces levels of sex hormone-binding globulin (SHBG), total and free testosterone, and inhibin B, while increasing the conversion of testosterone to estradiol [E2] due to heightened aromatase activity [82, 83]. This reduction in testosterone levels adversely affects spermatogenesis, as adequate testosterone levels are crucial for the attachment of Sertoli cells to developing germ cells. Furthermore, obesity can lead to epigenetic changes that may be passed down to future generations [84, 85].

Moreover, having too much visceral fat leads to the production of pro-inflammatory cytokines like interleukin-6 (IL-6) and tumor necrosis factor α (TNFα), which trigger low-grade systemic inflammation. In individuals with obesity, there's a disruption in the balance between oxidative and antioxidant systems, causing an uptick in ROS production. While ROS are crucial for normal spermatogenesis at controlled levels, excessive amounts can cause oxidation and damage to DNA, proteins, and lipids [86, 87].

Obesity also leads to insulin resistance, which in turn causes hyperinsulinemia. This condition reduces the liver's production of SHBG, resulting in elevated levels of E2. High levels of E2 suppress the hypothalamic-pituitary-gonadal axis, leading to decreased testosterone (T) production. Additionally, the production of adipokines is disrupted in individuals with obesity. Increased leptin secretion from adipose tissue, along with leptin resistance, negatively affects male fertility at both central and peripheral levels [88, 89]. The surplus of leptin reduces the secretion of gonadotropin-releasing hormone (GnRH), primarily by inhibiting kisspeptin neurons, which directly affects spermatogenesis. Thus, an excess of insulin and dysregulated adipokines negatively impact testicular function, leading to a "metabolic" form of male hypogonadism. However, research has shown a complex, two-way link between visceral adipose tissue dysfunction, systemic insulin resistance, and testicular issues. Notably, low testosterone levels further impair insulin sensitivity, encourage adipocyte growth, and increase body fat, perpetuating a vicious cycle [90, 91].

In the intricate web of molecular mechanisms behind obesity-induced male infertility, new molecules like sirtuins (SIRTs) are gaining attention. Recent studies indicate that SIRTs influence obesity and male fertility through various pathways [92, 93].

6. Weight Loss as a Therapeutic Strategy for Infertility in Obese Women

Weight loss presents a hopeful path for improving reproductive health in obese women. Various strategies for losing weight, including changes in lifestyle and medical treatments, have been investigated for their effectiveness in mitigating infertility caused by obesity [3, 94].

6.1. Pharmacological Interventions

Pharmacological treatments play a crucial role in overcoming the fertility issues related to obesity. Metformin, known primarily for its use in diabetes management, is celebrated for its ability to enhance insulin sensitivity. This attribute has proven effective in normalizing menstrual cycles and boosting ovulation rates among obese women. Beyond Metformin, glucagon-like peptide-1 (GLP-1) agonists, initially developed for managing type 2 diabetes, have shown promise [95, 96]. These agents have demonstrated efficacy in reducing insulin resistance associated with PCOS, a condition frequently seen in obese women. By improving insulin sensitivity, GLP-1 agonists may help in rectifying hormonal imbalances and enhancing fertility prospects. Furthermore, the use of antioxidants has been suggested as a viable approach to better reproductive outcomes in obese women. Research points to antioxidants like α-lipoic acid and myo-inositol as beneficial in

reducing oxidative stress within the oocyte environment, which could lead to improved fertility [97, 98]. The exploration doesn't stop here; attention is increasingly being directed towards medications that act on adipokines or their receptors. This includes investigating the effects of drugs that either boost adiponectin activity or raise its levels, given adiponectin's vital role in ovarian functionality and hormone secretion. Additionally, there's ongoing research into compounds that mitigate leptin resistance, a common challenge in obesity. Enhancing leptin sensitivity through such measures could significantly contribute to resolving various reproductive issues associated with obesity [99, 100].

6.2. Surgical Interventions

Surgical procedures, especially bariatric surgery, are increasingly acknowledged as an effective method for overcoming infertility issues in obese women. Bariatric surgery, aimed at achieving substantial weight loss, has demonstrated a beneficial effect on fertility. One study highlighted a significant improvement in infertility related to obesity after undergoing surgery. Further research establishes a connection between obesity and infertility, indicating that weight loss through surgery could be advantageous [101, 102]. A systematic review also points out that reducing weight in overweight or obese women can greatly improve the outcomes of fertility treatments. Moreover, studies shed light on the positive effects of bariatric surgery for obese women facing infertility who are trying to get pregnant, noting that the effectiveness of these surgical approaches may depend on various factors including age, the type of surgery performed, existing health conditions, and the patient's BMI prior to the surgery [103].

6.3. Lifestyle Modifications

Lifestyle adjustments have become a key treatment approach for tackling infertility in obese women. Programs aimed at weight reduction have shown to significantly boost fertility outcomes in various treatments. Specifically, for women with PCOS - a condition often linked to obesity and infertility, making lifestyle changes can improve reproductive capabilities by increasing insulin sensitivity and normalizing levels of luteinizing hormone. Moreover, focusing on reducing central obesity and combating insulin resistance is essential in addressing infertility associated with PCOS. A review of lifestyle factors among those seeking infertility treatment highlighted the advantages of intensive lifestyle modification programs in managing weight and enhancing fertility results. In addition, exercise programs, compared to diet-only interventions, have proven effective in treating anovulatory infertility in obese women with PCOS [104, 105].

7. Conclusion

Obesity is a complex metabolic condition that profoundly affects reproductive health in both sexes. In women, excessive adiposity disrupts the hypothalamic–pituitary–gonadal axis, impairs oocyte maturation, and alters ovarian responsiveness to fertility treatments. In men, obesity contributes to hypogonadism, poor semen parameters, and increased oxidative stress, collectively diminishing reproductive potential. These alterations are mediated through insulin resistance, dysregulated adipokine signaling, mitochondrial dysfunction, and endoplasmic reticulum stress.

Weight reduction remains the cornerstone of therapy, with lifestyle modification offering substantial benefits when sustained over time. Pharmacological agents such as metformin and GLP-1 agonists, along with bariatric surgery, provide effective adjunctive options that improve hormonal balance, gamete quality, and fertility outcomes.

Future research should focus on elucidating sex-specific molecular mechanisms linking obesity and infertility and on optimizing personalized therapeutic strategies. Addressing obesity not only enhances reproductive outcomes but also contributes to broader metabolic and psychological well-being, reinforcing the necessity of holistic interventions in reproductive medicine.

References

[1] D. Khanna, B. Welch, and A. Rehman, *Pathophysiology of obesity*. Treasure Island: StatPearls Publishing, 2025.

[2] S. K. Ahmed and R. A. Mohammed, "Obesity: Prevalence, causes, consequences, management, preventive strategies and future research directions," *Metabolism Open*, p. 100375, 2025. https://doi.org/10.1016/j.metop.2025.100375

[3] L. Zheng, L. Yang, Z. Guo, N. Yao, S. Zhang, and P. Pu, "Obesity and its impact on female reproductive health: Unraveling the connections," *Frontiers in Endocrinology*, vol. 14, p. 1326546, 2024. https://doi.org/10.3389/fendo.2023.1326546

[4] S. Medenica *et al.*, "Female infertility in the era of obesity: The clash of two pandemics or inevitable consequence?," *Clinical Endocrinology*, vol. 98, no. 2, pp. 141-152, 2023. https://doi.org/10.1111/cen.14785

[5] S. Lim, C. Harrison, E. Callander, R. Walker, H. Teede, and L. Moran, "Addressing obesity in preconception, pregnancy, and postpartum: a review of the literature," *Current Obesity Reports*, vol. 11, no. 4, pp. 405-414, 2022.

[6] C. Voros *et al.*, "The relationship between obesity, bariatric surgery, and infertility: A systematic review," *Life*, vol. 15, no. 5, p. 758, 2025. https://doi.org/10.3390/life15050758

[7] M. Rafique, A. Al-Badr, A. Saleh, and D. H. Al-Jaroudi, "Economic perspective of evaluating fertility treatment in obese and overweight infertile women," *Saudi Medical Journal*, vol. 42, no. 6, p. 666, 2021.

[8] D. Gautam *et al.*, "The challenges of obesity for fertility: A FIGO literature review," *International Journal of Gynecology & Obstetrics*, vol. 160, pp. 50-55, 2023.

[9] R. Kurzrock and P. R. Cohen, "Polycystic ovary syndrome in men: Stein–Leventhal syndrome revisited," *Medical Hypotheses*, vol. 68, no. 3, pp. 480-483, 2007.

[10] E. Y. Adashi, D. Cibula, M. Peterson, and R. Azziz, "The polycystic ovary syndrome: the first 150 years of study," *F&S Reports*, vol. 4, no. 1, pp. 2-18, 2023.

[11] C. R. Giviziez, E. G. Sanchez, M. S. Approbato, M. C. Maia, E. A. B. Fleury, and R. S. Sasaki, "Obesity and anovulatory infertility: A review," *JBRA assisted reproduction*, vol. 20, no. 4, p. 240, 2016.

[12] I. Iavarone *et al.*, "Obesity may impair response to ovarian stimulation. A retrospective observational study on oocyte quality," *Frontiers in Cell and Developmental Biology*, vol. 12, p. 1461132, 2024.
[13] K. Itriyeva, "The effects of obesity on the menstrual cycle," *Current Problems in Pediatric and Adolescent Health Care*, vol. 52, no. 8, p. 101241, 2022.
[14] Y. He *et al.*, "Associations of childhood adiposity with menstrual irregularity and polycystic ovary syndrome in adulthood: the Childhood Determinants of Adult Health Study and the Bogalusa Heart Study," *Human Reproduction*, vol. 35, no. 5, pp. 1185-1198, 2020.
[15] H. Cena, L. Chiovato, and R. E. Nappi, "Obesity, polycystic ovary syndrome, and infertility: A new avenue for GLP-1 receptor agonists," *The Journal of Clinical Endocrinology & Metabolism*, vol. 105, no. 8, pp. e2695-e2709, 2020.
[16] W. Su, L. Zhang, J. Cheng, Y. Fu, J. Zhao, and H. Chen, "Impact of BMI on pregnancy outcomes in PCOS patients undergoing ultralong GnRH—a protocol with blastocyst transfer," *European Journal of Medical Research*, vol. 30, no. 1, p. 849, 2025.
[17] D. Liu, X. Luo, and K. Zhou, "Association between current relative fat mass and history of female infertility based on the NHANES survey," *Scientific Reports*, vol. 15, no. 1, p. 6294, 2025.
[18] G. A. Only, "Obesity and reproduction: A committee opinion," *Fertility and Sterility*, vol. 116, no. 5, pp. 1266-1285, 2021.
[19] T. M. Barber, P. Hanson, M. O. Weickert, and S. Franks, "Obesity and polycystic ovary syndrome: Implications for pathogenesis and novel management strategies," *Clinical Medicine Insights: Reproductive Health*, vol. 13, p. 1179558119874042, 2019.
[20] J. Bila *et al.*, "Obesity as a part of polycysric ovary syndrome (pcos)—a review of pathophysiology and comprehensive therapeutic strategies," *Journal of Clinical Medicine*, vol. 14, no. 16, p. 5642, 2025.
[21] R. S. Legro, "Obesity and PCOS: Implications for diagnosis and treatment," *Seminars in Reproductive Medicine*, vol. 30, no. 06, pp. 496-506, 2012.
[22] A. M. Z. Jukic, C. R. Weinberg, A. J. Wilcox, D. R. McConnaughey, P. Hornsby, and D. D. Baird, "Accuracy of reporting of menstrual cycle length," *American Journal of Epidemiology*, vol. 167, no. 1, pp. 25-33, 2008.
[23] Y. M. Mittiku, H. Mekonen, G. Wogie, M. A. Tizazu, and G. E. Wake, "Menstrual irregularity and its associated factors among college students in Ethiopia, 2021," *Frontiers in Global Women's Health*, vol. 3, p. 917643, 2022.
[24] E. H. Yeung *et al.*, "Adiposity and sex hormones across the menstrual cycle: The BioCycle Study," *International Journal of Obesity*, vol. 37, no. 2, pp. 237-243, 2013.
[25] K. Barbouni *et al.*, "When weight matters: How obesity impacts reproductive health and pregnancy-a systematic review," *Current Obesity Reports*, vol. 14, no. 1, p. 37, 2025. https://doi.org/10.1007/s13679-025-00629-9
[26] H. Ding *et al.*, "Resistance to the insulin and elevated level of androgen: A major cause of polycystic ovary syndrome," *Frontiers in Endocrinology*, vol. 12, p. 741764, 2021.
[27] M. A. Sanchez-Garrido and M. Tena-Sempere, "Metabolic dysfunction in polycystic ovary syndrome: Pathogenic role of androgen excess and potential therapeutic strategies," *Molecular Metabolism*, vol. 35, p. 100937, 2020.
[28] J. Rojas *et al.*, "Polycystic ovary syndrome, insulin resistance, and obesity: navigating the pathophysiologic labyrinth," *International Journal of Reproductive Medicine*, vol. 2014, no. 1, p. 719050, 2014.
[29] M. Waters and P. Tadi, "Genetics, female gametogenesis in StatPearls," Treasure Island (FL): StatPearls Publishing, 2022. https://www.ncbi.nlm.nih.gov/books/NBK555917/
[30] R. Oliver and H. Basit, "Embryology, fertilization," Treasure Island (FL): StatPearls Publishing, 2023. https://www.ncbi.nlm.nih.gov/books/NBK542186/
[31] E. Cox and V. Takov, "Embryology, ovarian follicle development," StatPearls Publishing, 2025. https://www.ncbi.nlm.nih.gov/books/NBK532300/
[32] Y.-X. Liu *et al.*, "Regulation of follicular development and differentiation by intra-ovarian factors and endocrine hormones," *Frontiers in Bioscience-Landmark*, vol. 24, no. 5, pp. 983-993, 2019.
[33] A. Arroyo, B. Kim, and J. Yeh, "Luteinizing hormone action in human oocyte maturation and quality: signaling pathways, regulation, and clinical impact," *Reproductive Sciences*, vol. 27, no. 6, pp. 1223-1252, 2020.
[34] Z. Pei, K. Deng, C. Xu, and S. Zhang, "The molecular regulatory mechanisms of meiotic arrest and resumption in Oocyte development and maturation," *Reproductive Biology and Endocrinology*, vol. 21, no. 1, p. 90, 2023.
[35] M. He, T. Zhang, Y. Yang, and C. Wang, "Mechanisms of oocyte maturation and related epigenetic regulation," *Frontiers in Cell and Developmental Biology*, vol. 9, p. 654028, 2021.
[36] C. Jessus, C. Munro, and E. Houliston, "Managing the oocyte meiotic arrest—Lessons from frogs and jellyfish," *Cells*, vol. 9, no. 5, p. 1150, 2020.
[37] W. Yong, J. Wang, Y. Leng, L. Li, and H. Wang, "Role of obesity in female reproduction," *International Journal of Medical Sciences*, vol. 20, no. 3, p. 366, 2023.
[38] K. A. Reynolds, A. L. Boudoures, M. M.-Y. Chi, Q. Wang, and K. H. Moley, "Adverse effects of obesity and/or high-fat diet on oocyte quality and metabolism are not reversible with resumption of regular diet in mice," *Reproduction, Fertility and Development*, vol. 27, no. 4, pp. 716-724, 2015.
[39] M. W. Elting, P. Suresh, and S. Dumont, "The spindle: Integrating architecture and mechanics across scales," *Trends in Cell Biology*, vol. 28, no. 11, pp. 896-910, 2018.
[40] M. Aboelenain, K. Schindler, and C. S. Blengini, "Evaluation of the spindle assembly checkpoint integrity in mouse oocytes," *Journal of Visualized Experiments*, no. 187, p. 10.3791/64459, 2022.
[41] W. F. A. Marei *et al.*, "Differential effects of high fat diet-induced obesity on oocyte mitochondrial functions in inbred and outbred mice," *Scientific Reports*, vol. 10, no. 1, p. 9806, 2020. https://doi.org/10.1038/s41598-020-66702-6
[42] M. Lee *et al.*, "Diet-induced obesity alters granulosa cell transcriptome and ovarian immune environment in mice," *Life*, vol. 15, no. 3, p. 330, 2025.
[43] G. M. Baldini *et al.*, "Abnormalities of oocyte maturation: Mechanisms and implications," *International Journal of Molecular Sciences*, vol. 25, no. 22, p. 12197, 2024.
[44] Ş. Hatırnaz *et al.*, "Oocyte maturation abnormalities-A systematic review of the evidence and mechanisms in a rare but difficult to manage fertility pheneomina," *Turkish Journal of Obstetrics and Gynecology*, vol. 19, no. 1, p. 60, 2022.
[45] L. Han *et al.*, "Increased mtDNA mutation frequency in oocytes causes epigenetic alterations and embryonic defects," *National Science Review*, vol. 9, no. 10, p. nwac136, 2022.

[46] S. Long *et al.*, "Maintaining mitochondrial DNA copy number mitigates ROS-induced oocyte decline and female reproductive aging," *Communications Biology*, vol. 7, no. 1, p. 1229, 2024.
[47] E. Babayev and E. Seli, "Oocyte mitochondrial function and reproduction," *Current Opinion in Obstetrics and Gynecology*, vol. 27, no. 3, pp. 175-181, 2015. https://doi.org/10.1097/GCO.0000000000000164
[48] T. Wang *et al.*, "Mitochondrial dysfunction in oocytes:Implications for fertility and ageing," *Journal of Ovarian Research*, vol. 18, no. 1, p. 186, 2025. https://doi.org/10.1186/s13048-025-01764-6
[49] N. M. Grindler and K. H. Moley, "Maternal obesity, infertility and mitochondrial dysfunction: Potential mechanisms emerging from mouse model systems," *MHR: Basic Science of Reproductive Medicine*, vol. 19, no. 8, pp. 486-494, 2013.
[50] H. Song *et al.*, "The regulatory role of adipocyte mitochondrial homeostasis in metabolism-related diseases," *Frontiers in Physiology*, vol. 14, p. 1261204, 2023.
[51] L. L. Wu *et al.*, "Mitochondrial dysfunction in oocytes of obese mothers: Transmission to offspring and reversal by pharmacological endoplasmic reticulum stress inhibitors," *Development*, vol. 142, no. 4, pp. 681-691, 2015. https://doi.org/10.1242/dev.114850
[52] C. Boots, A. Boudoures, W. Zhang, A. Drury, and K. Moley, "Obesity-induced oocyte mitochondrial defects are partially prevented and rescued by supplementation with co-enzyme Q10 in a mouse model," *Human Reproduction*, vol. 31, no. 9, pp. 2090-2097, 2016. https://doi.org/10.1093/humrep/dew181
[53] A. Elias-Lopez, O. Vázquez-Mena, and A. Sferruzzi-Perri, "Mitochondrial dysfunction in the offspring of obese mothers and it's transmission through damaged oocyte mitochondria: Integration of mechanisms," *Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease*, vol. 1869, no. 7, p. 166802, 2023.
[54] B. Meulders, W. F. Marei, I. Xhonneux, L. Loier, A. Smits, and J. L. Leroy, "Preconception diet interventions in obese outbred mice and the impact on female offspring metabolic health and oocyte quality," *International Journal of Molecular Sciences*, vol. 25, no. 4, p. 2236, 2024.
[55] D. Mekahli, G. Bultynck, J. B. Parys, H. De Smedt, and L. Missiaen, "Endoplasmic-reticulum calcium depletion and disease," *Cold Spring Harbor Perspectives in Biology*, vol. 3, no. 6, p. a004317, 2011.
[56] X. Chen, C. Shi, M. He, S. Xiong, and X. Xia, "Endoplasmic reticulum stress: Molecular mechanism and therapeutic targets," *Signal Transduction and Targeted Therapy*, vol. 8, no. 1, p. 352, 2023. https://doi.org/10.1038/s41392-023-01570-w
[57] S. Liong and M. Lappas, "Endoplasmic reticulum stress is increased in adipose tissue of women with gestational diabetes," *PloS one*, vol. 10, no. 4, p. e0122633, 2015. https://doi.org/10.1371/journal.pone.0122633
[58] D. Chowdhury, C. E. Jang, P. Lajoie, and S. J. Renaud, "A stress paradox: The dual role of the unfolded protein response in the placenta," *Frontiers in Endocrinology*, vol. 15, p. 1525189, 2024. https://doi.org/10.3389/fendo.2024.1525189
[59] I. M. Saadeldin, S. Ehab, M. E. F. Alshammari, A. M. Abdelazim, and A. M. Assiri, "The mammalian oocyte: A central hub for cellular reprogramming and stemness," *Stem Cells and Cloning: Advances and Applications*, vol. 18, pp. 15-34, 2025. https://doi.org/10.2147/SCCAA.S513982
[60] T. Lin, J. E. Lee, J. W. Kang, H. Y. Shin, J. B. Lee, and D. I. Jin, "Endoplasmic reticulum (ER) stress and unfolded protein response (UPR) in mammalian oocyte maturation and preimplantation embryo development," *International Journal of Molecular Sciences*, vol. 20, no. 2, p. 409, 2019. https://doi.org/10.3390/ijms20020409
[61] L. L. Wu, D. L. Russell, R. J. Norman, and R. L. Robker, "Endoplasmic reticulum (ER) stress in cumulus-oocyte complexes impairs pentraxin-3 secretion, mitochondrial membrane potential (ΔΨm), and embryo development," *Molecular Endocrinology*, vol. 26, no. 4, pp. 562-573, 2012. https://doi.org/10.1210/me.2011-1362
[62] X. Xu, Y. Pang, and X. Fan, "Mitochondria in oxidative stress, inflammation and aging: From mechanisms to therapeutic advances," *Signal Transduction and Targeted Therapy*, vol. 10, no. 1, p. 190, 2025. https://doi.org/10.1038/s41392-025-02253-4
[63] S. Pandey, S. Pandey, A. Maheshwari, and S. Bhattacharya, "The impact of female obesity on the outcome of fertility treatment," *Journal of Human Reproductive Sciences*, vol. 3, no. 2, pp. 62-67, 2010. https://doi.org/10.4103/0974-1208.69332
[64] C. L. Chang, "Facilitation of ovarian response by mechanical force—Latest insight on fertility improvement in women with poor ovarian response or primary ovarian insufficiency," *International Journal of Molecular Sciences*, vol. 24, no. 19, p. 14751, 2023. https://doi.org/10.3390/ijms241914751
[65] R. S. Sasaki, M. S. Approbato, M. C. Maia, E. A. F. e Ferreira, and N. Zanluchi, "Ovulatory status of overweight women without polycystic ovary syndrome," *JBRA Assisted Reproduction*, vol. 23, no. 1, p. 2, 2019. https://doi.org/10.5935/1518-0557.20180071
[66] Y. Zeng *et al.*, "Clomiphene citrate reduces premature LH surge in obese women during controlled ovarian stimulation: A retrospective cohort study," *Frontiers in Endocrinology*, vol. 16, p. 1512821, 2025. https://doi.org/10.3389/fendo.2025.1512821
[67] S. Jiang and Y. Kuang, "Clomiphene citrate is associated with favorable cycle characteristics but impaired outcomes of obese women with polycystic ovarian syndrome undergoing ovarian stimulation for in vitro fertilization," *Medicine*, vol. 96, no. 32, p. e7540, 2017. https://doi.org/10.1097/MD.0000000000007540
[68] Q. Chang, S. Wang, Q. Mai, and C. Zhou, "Impact of obesity on proteomic profiles of follicular fluid-derived small extracellular vesicles: A comparison between PCOS and non-PCOS women," *Journal of Ovarian Research*, vol. 18, no. 1, p. 121, 2025. https://doi.org/10.1186/s13048-025-01703-5
[69] J. Song, S. Xiang, C. Pang, J. Guo, and Z. Sun, "Metabolomic alternations of follicular fluid of obese women undergoing in-vitro fertilization treatment," *Scientific Reports*, vol. 10, no. 1, p. 5968, 2020. https://doi.org/10.1038/s41598-020-62975-z
[70] S. Hallisey *et al.*, "The association of obesity with euploidy rates in women undergoing in vitro fertilization with preimplantation genetic testing," *Journal of Assisted Reproduction and Genetics*, vol. 39, no. 11, pp. 2521-2528, 2022. https://doi.org/10.1007/s10815-022-02624-8
[71] L. A. Kassi *et al.*, "Body mass index, not race, may be associated with an alteration in early embryo morphokinetics during in vitro fertilization," *Journal of Assisted Reproduction and Genetics*, vol. 38, no. 12, pp. 3091-3098, 2021. https://doi.org/10.1007/s10815-021-02350-7
[72] C. Brunet *et al.*, "Impact of women obesity and obesity severity on live birth rate after in vitro fertilization," *Journal of Clinical Medicine*, vol. 9, no. 8, p. 2414, 2020. https://doi.org/10.3390/jcm9082414

[73] Y. Wan *et al.*, "IGF2 reduces meiotic defects in oocytes from obese mice and improves embryonic developmental competency," *Reproductive Biology and Endocrinology*, vol. 20, no. 1, p. 101, 2022. https://doi.org/10.1186/s12958-022-00972-9

[74] R. Malhotra, J. G. de Paredes, A. Smith, A. Chemerinski, D. Doshi, and S. S. Morelli, "Obesity epidemic and its impact on female fertility: Current understanding and future directions," *Cureus*, vol. 17, no. 7, p. e87283, 2025. https://doi.org/10.7759/cureus.87283

[75] S. Chauvin, "Role of granulosa cell dysfunction in women infertility associated with polycystic ovary syndrome and obesity," *Biomolecules*, vol. 15, no. 7, p. 923, 2025. https://doi.org/10.3390/biom15070923

[76] N. O. Palmer, H. W. Bakos, T. Fullston, and M. Lane, "Impact of obesity on male fertility, sperm function and molecular composition," *Spermatogenesis*, vol. 2, no. 4, pp. 253-263, 2012. https://doi.org/10.4161/spmg.21362

[77] R. Ahmad and M. Haque, "Obesity: A doorway to a molecular path leading to infertility," *Cureus*, vol. 14, no. 10, p. e30770, 2022. https://doi.org/10.7759/cureus.30770

[78] C. A. Service, D. Puri, S. Al Azzawi, T.-C. Hsieh, and D. P. Patel, "The impact of obesity and metabolic health on male fertility: A systematic review," *Fertility and Sterility*, vol. 120, no. 6, pp. 1098-1111, 2023. https://doi.org/10.1016/j.fertnstert.2023.10.017

[79] G. Bellastella *et al.*, "How much does obesity affect the male reproductive function?," *International Journal of Obesity Supplements*, vol. 9, no. 1, pp. 50-64, 2019. https://doi.org/10.1038/s41367-019-0008-2

[80] Y. Kang *et al.*, "Progress in investigating the impact of obesity on male reproductive function," *Biomedicines*, vol. 13, no. 9, p. 2054, 2025. https://doi.org/10.3390/biomedicines13092054

[81] S. Wang *et al.*, "Influence of body mass index and waist–hip ratio on male semen parameters in infertile men in the real world: a retrospective study," *Frontiers in Endocrinology*, vol. 14, p. 1148715, 2023. https://doi.org/10.3389/fendo.2023.1148715

[82] F. Barbagallo *et al.*, "Molecular mechanisms underlying the relationship between obesity and male infertility," *Metabolites*, vol. 11, no. 12, p. 840, 2021. https://doi.org/10.3390/metabo11120840

[83] M. Darand, Z. Salimi, M. Ghorbani, N. Sadeghi, S. Babaie, and M. Hosseinzadeh, "Obesity is associated with quality of sperm parameters in men with infertility: A cross-sectional study," *Reproductive Health*, vol. 20, no. 1, p. 134, 2023. https://doi.org/10.1186/s12978-023-01664-2

[84] G. Raad, M. Hazzouri, S. Bottini, M. Trabucchi, J. Azoury, and V. Grandjean, "Paternal obesity: How bad is it for sperm quality and progeny health?," *Basic and Clinical Andrology*, vol. 27, no. 1, p. 20, 2017. https://doi.org/10.1186/s12610-017-0064-9

[85] R. Barakat *et al.*, "Germline-dependent transmission of male reproductive traits induced by an endocrine disruptor, di-2-ethylhexyl phthalate, in future generations," *Scientific Reports*, vol. 10, no. 1, p. 5705, 2020. https://doi.org/10.1038/s41598-020-62584-w

[86] A. Chait and L. J. Den Hartigh, "Adipose tissue distribution, inflammation and its metabolic consequences, including diabetes and cardiovascular disease," *Frontiers in Cardiovascular Medicine*, vol. 7, p. 522637, 2020. https://doi.org/10.3389/fcvm.2020.00022

[87] G. Shimi, M. H. Sohouli, A. Ghorbani, A. Shakery, and H. Zand, "The interplay between obesity, immunosenescence, and insulin resistance," *Immunity & Ageing*, vol. 21, no. 1, p. 13, 2024. https://doi.org/10.1186/s12979-024-00414-7

[88] M. S. Lonardo *et al.*, "Hypothalamic-ovarian axis and adiposity relationship in polycystic ovary syndrome: Physiopathology and therapeutic options for the management of metabolic and inflammatory aspects," *Current Obesity Reports*, vol. 13, no. 1, pp. 51-70, 2024. https://doi.org/10.1007/s13679-023-00531-2

[89] E. J. Houston and N. M. Templeman, "Reappraising the relationship between hyperinsulinemia and insulin resistance in PCOS," *Journal of Endocrinology*, vol. 265, no. 2, p. e240269, 2025. https://doi.org/10.1530/JOE-24-0269

[90] V. Muraleedharan and T. H. Jones, "Testosterone and the metabolic syndrome," *Therapeutic Advances in Endocrinology and Metabolism*, vol. 1, no. 5, pp. 207-223, 2010. https://doi.org/10.1177/2042018810390258

[91] S. C. Pereira, L. Crisóstomo, M. Sousa, P. F. Oliveira, and M. G. Alves, "Metabolic diseases affect male reproduction and induce signatures in gametes that may compromise the offspring health," *Environmental Epigenetics*, vol. 6, no. 1, p. dvaa019, 2020. https://doi.org/10.1093/eep/dvaa019

[92] D. C. André, P. F. Oliveira, M. G. Alves, and A. D. Martins, "Caloric restriction and sirtuins as new players to reshape male fertility," *Metabolites*, vol. 15, no. 5, p. 303, 2025. https://doi.org/10.3390/metabo15050303

[93] B. T. George, M. Jhancy, R. Dube, S. S. Kar, and L. M. Annamma, "The molecular basis of male infertility in obesity: A literature review," *International Journal of Molecular Sciences*, vol. 25, no. 1, p. 179, 2023. https://doi.org/10.3390/ijms25010179

[94] K. Sim, S. R. Partridge, and A. Sainsbury, "Does weight loss in overweight or obese women improve fertility treatment outcomes? A systematic review," *Obesity Reviews*, vol. 15, no. 10, pp. 839-850, 2014. https://doi.org/10.1111/obr.12217

[95] J. Drzewoski and M. Hanefeld, "The current and potential therapeutic use of metformin—the good old drug," *Pharmaceuticals*, vol. 14, no. 2, p. 122, 2021. https://doi.org/10.3390/ph14020122

[96] M. A. Sánchez-Garrido *et al.*, "Superior metabolic improvement of polycystic ovary syndrome traits after GLP1-based multi-agonist therapy," *Nature Communications*, vol. 15, no. 1, p. 8498, 2024. https://doi.org/10.1038/s41467-024-52898-y

[97] B. Austregésilo de Athayde De Hollanda Morais *et al.*, "The efficacy and safety of GLP-1 agonists in PCOS women living with obesity in promoting weight loss and hormonal regulation: A meta-analysis of randomized controlled trials," *Journal of Diabetes and its Complications*, vol. 38, no. 10, p. 108834, 2024. https://doi.org/10.1016/j.jdiacomp.2024.108834

[98] B. H. Hoteit *et al.*, "The dual impact of GLP-1 receptor agonists on metabolic and reproductive health in polycystic ovary syndrome: insights from human and animal trials," *Therapeutic Advances in Endocrinology and Metabolism*, vol. 16, p. 20420188251383064, 2025. https://doi.org/10.1177/20420188251383064

[99] N. Ramakrishnan, K. Auger, N. Rahimi, and I. Jialal, "Biochemistry, adiponectin. StatPearls [Internet]." Treasure Island, FL: StatPearls Publishing, 2023.

[100] A. Barbe *et al.*, "Mechanisms of adiponectin action in fertility: An overview from gametogenesis to gestation in humans and animal models in normal and pathological conditions," *International Journal of Molecular Sciences*, vol. 20, no. 7, p. 1526, 2019. https://doi.org/10.3390/ijms20071526

[101] B. R. Makhsosi, P. Ghobadi, M. Otaghi, and Z. Tardeh, "Impact of bariatric surgery on infertility in obese women: a systematic review and meta-analysis," *Annals of Medicine and Surgery,* vol. 86, no. 12, pp. 7042-7048, 2024. https://doi.org/10.1097/MS9.0000000000002657

[102] H. Almutairi *et al.*, "The Effectiveness of Bariatric Surgery on Treating Infertility in Women—A Systematic Review and Meta-Analysis," *Journal of Clinical Medicine,* vol. 13, no. 18, p. 5569, 2024. https://doi.org/10.3390/jcm13185569

[103] Database of Abstracts of Reviews of Effects (DARE), "Quality-assessed reviews [Internet]. York (UK): Centre for reviews and dissemination (UK); 1995-. Does weight loss in overweight or obese women improve fertility treatment outcomes? A systematic review," 2014. https://www.ncbi.nlm.nih.gov/books/NBK292171/

[104] A. Sustarsic *et al.*, "The influence of lifestyle interventions and overweight on infertility: a systematic review, meta-analysis, and meta-regression of randomized controlled trials," *Frontiers in Medicine,* vol. 10, p. 1264947, 2023. https://doi.org/10.3389/fmed.2023.1264947

[105] S. S. Lim, S. K. Hutchison, E. Van Ryswyk, R. J. Norman, H. J. Teede, and L. J. Moran, "Lifestyle changes in women with polycystic ovary syndrome," *Cochrane Database of Systematic Reviews,* vol. 3, no. 3, p. CD007506, 2019. https://doi.org/10.1002/14651858.CD007506.pub4