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Is obesity a contributing factor to female infertility? - a literature review

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Keywords: infertility, obesity, PCOS, adipokines, lifestyle interventions

Abstract

Introduction and purpose: Obesity has emerged as one of the most pressing public health issues worldwide, with significant implications for female reproductive health. This review examines the complex relationship between obesity and infertility, emphasizing how obesity disrupts hormonal balance, metabolic processes, and ovarian function, leading to infertility.
Material and methods: Medical databases like PubMed and Google Scholar were searched for scientific papers on impact of obesity on female infertility. These were analyzed and summarized in this review.
State of knowledge: The hormonal imbalances associated with obesity, such as insulin resistance and elevated androgen levels, are closely linked to ovulation disorders, particularly in conditions like polycystic ovarian syndrome (PCOS). Furthermore, obesity negatively impacts oocyte quality, endometrial receptivity, and the success of assisted reproductive technologies (ART), such as in vitro fertilization (IVF). The review also explores potential interventions, including lifestyle modifications, pharmacological treatments, and bariatric surgery, to improve fertility outcomes in obese women.

Conclusion: Addressing obesity is crucial in managing female infertility, and an integrative approach combining prevention, treatment, and ART advancements is essential for improving reproductive health. This work underscores the need for continued research and multidisciplinary collaboration to optimize fertility outcomes for obese women.

Keywords
infertility, obesity, PCOS, adipokines, lifestyle interventions

Introduction and purpose

Obesity became one of the most important health problems in contemporary times. The American Medical Association confirmed that obesity should be regarded as disease itself in 2013 [1]. Research says that almost one third of the world is overweight or obese meaning that over 2 billion people [2] are associated with a higher risk of many diseases such as hypertension, coronary heart disease or neoplasm [3]. In our research we would like to emphasise obesity's impact on female reproductive system. It is one of the main reasons for infertility in women. Changes of hormones such as insulin, estrogen and gonadotropins lead to many severe conditions like polycystic ovarian syndrome (PCOS) [4] or menstrual cycle disorders. Excessive secretion of proinflammatory adipokines in obese women inhibits hypothalamic-pituitary-ovarian axis which leads to ovulation disorders and infertility. All factors described above, lipids accumulation and inflammation contribute to elongated time-to-pregnancy. Therefore, diagnosing and treating obesity is one of the most significant objectives for physicians to achieve. Lifestyle changes and physical activity in obese women showed effectiveness in infertility treatment.

State of knowledge

1. Obesity - definition and epidemiology

Obesity is defined as the pathological accumulation of adipose tissue in the body associating with an increased risk of chronic diseases such as diabetes type 2, hyperlipidemia, heart diseases, osteoporosis, infertility and increased probability of certain cancers (e.g. colorectal cancer), according to the World Health Organization [5,6]. The main cause of obesity is chronic positive energy balance when more calories are taken than exploited in the body [5]. About 12,5% of people in the world are living with obesity and it has doubled since 1990. Moreover, 390 million children and adolescents were overweight, including 160 million with obesity. The diagnosis of obesity is based on measuring people's weight and height and by calculating the body mass index (BMI): weight (kg)/height² (m^2) [6]. Obesity in adults is defined as a BMI greater than or equal to 30. The visceral obesity should be diagnosed based on patients' waist circumference - more than 80 cm in females or 94 cm in males [7]. Waist circumference is measured by determining the midpoint between the lower point of the rib cage and the iliac crest (according to WHO) or higher border of the iliac crest (according to NIH) [8]. The bioimpedance method of checking fat mass percentage of the body is another option for diagnosing obesity - >25% in males and >35% in females [7]. The epidemiology of obesity depends on the region: 31% in the WHO South-East Asia Region and the African Region to 67% in the Region of the Americas [6].

2. Influence of obesity in female infertility

Obesity's influence on female infertility has been widely researched, with many studies identifying its negative impact on reproductive health.

Obesity disrupts hormonal balance, increases inflammation, and causes metabolic disturbances that hinder fertility. Zheng's et al. emphasize the importance of understanding these mechanisms and their effects on oocyte quality, endometrial receptivity, and overall reproductive success. It also underscores the potential benefits of targeted therapeutic strategies, such as weight loss, in improving fertility outcomes in obese women.

The interplay between obesity and female infertility is a complex and multifaceted issue that profoundly affects reproductive health. Biological, hormonal, and metabolic pathways disrupted by obesity shed light on how chronic inflammation, oxidative stress, and hormonal imbalances compromise oocyte quality, endometrial receptivity, and overall reproductive function [9].

2.1 Obesity and PCOS

Polycystic Ovary Syndrome (PCOS) is the most common endocrine disorder affecting women of reproductive age and is commonly associated with obesity and overweight. Obesity is also linked to insulin resistance and hyperandrogenemia [10]. Obese women with PCOS are at increased risk of developing insulin resistance, hyperinsulinemia, and type 2 diabetes. Hyperinsulinemia stimulates excessive androgen production in the ovaries [9]. Insulin resistance and hyperinsulinemia resulting from obesity contribute to hyperandrogenemia also by inhibiting hepatic production of sex hormone-binding globulin (SHBG) [11]. As a result, these androgens are aromatized to estrogens in the excessive adipose tissue. This mechanism contributes to a negative feedback loop within the hypothalamic-pituitary-ovarian (HPO) axis, disrupting normal gonadotropin secretion [12] that is essential for normal follicle growth and ovulatory function [11] .

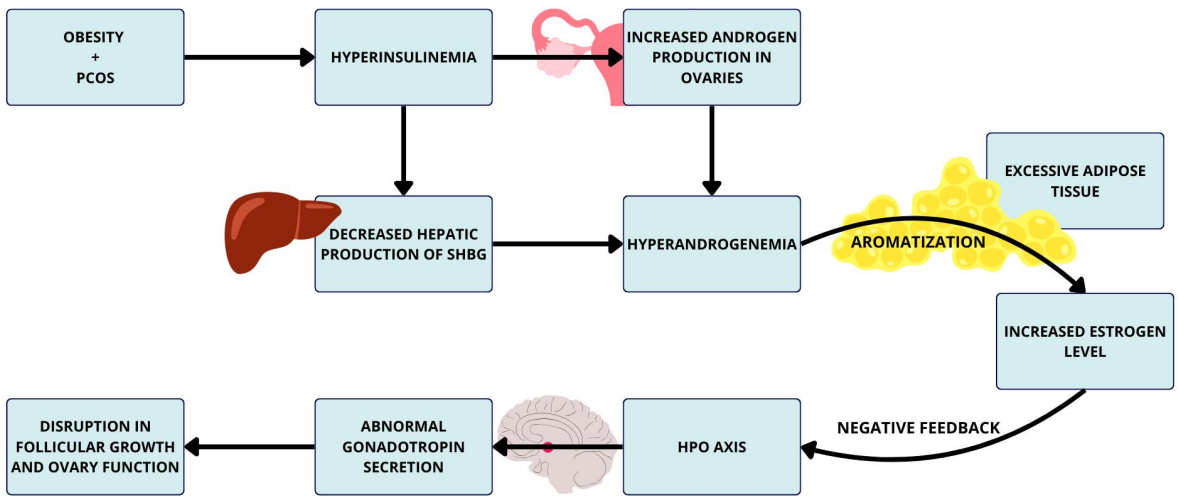

Fig 1. Processes leading from PCOS with obesity to disruptions in follicle growth and ovulatory function

2.2 Adipokines

White adipose tissue functions as an endocrine organ, influencing glucose and lipid metabolism as well as reproductive processes through the secretion of adipokines. Adipokines, acting as hormones, cause inflammation, metabolic disturbances, and impaired cell function, affecting sexual maturation and fertility [10].

Leptin affects reproductive function because of its influence on hypothalamus by initiating reproductive maturation and maintaining proper hypothalamic-pituitary-ovarian axis signaling. Interestingly, in the menstrual cycle, levels of leptin and tumor necrosis factor-alfa (TNF-α) vary between follicular and luteal phase, although the impact of this phenomenon is not yet known but it is possible that this affects signaling within the HPO axis [11]. As previously mentioned, the HPO axis is crucial for maintaining female reproductive health [9]. Leptin inhibits insulin-induced ovarian steroidogenesis and LH-stimulated estradiol production. Moreover, leptin regulates early embryo development, potentially explaining poor reproductive outcomes in obese women.

Adiponectin increases insulin sensitivity by enhancing hepatic and muscle glucose uptake and decreasing gluconeogenesis in the liver [10]. Hypoadiponectinemia has been identified as a potential mechanism contributing to insulin resistance in obesity and type 2 diabetes[13]. Hypoadiponectinemia also leads to insulinemia and hyperandrogenemia. Unlike the other adipokines, levels of adiponectin are decreased in obese women.

Visfatin has been reported to have insulin-mimetic increasing muscle glucose uptake and decreasing glucose release from hepatocytes. Another adipokine, chemerin, affects reproductive functions by impairing follicle stimulating hormone (FSH)-induced follicular steroidogenesis [10] .

2.3 Obesity and inflammation

Adipose tissue, a primary contributor to chronic inflammation, generates pro-inflammatory cytokines and exacerbates oxidative stress, perpetuating a cycle that undermines oocyte viability and endometrial health. Pro-inflammatory molecules that are produced by adipose tissue are TNF-α and IL-6 [9]. Despite the fact that oxidative stimulation plays an important role in oocyte maturation, oxidative stress may increase the risk of poor oocyte quality and induce oocyte apoptosis [14]. What is more, oxidative stress is associated with PCOS,

preeclampsia and endometriosis [15]. The inflammation can also negatively affect the endometrial lining leading to reduction of receptivity to embryo implantation [9].

2.4 Obesity and Lipid metabolism

Obesity is characterized by elevated triglyceride levels and decreased high-density lipoprotein cholesterol (HDL-C), leading to lipid accumulation and oxidative stress. These lipid abnormalities and the associated cellular stress affect the reproductive system by impairing granulosa cell function and mitochondrial efficiency, which are essential for oocyte maturation and embryo development [9].

2.5 Obesity and Time-to-Pregnancy

The Danish internet-based prospective cohort study revealed longer time-to-pregnancy (TTP) among obese and overweight women in comparison to normal weight ones, which is consistent with the findings of numerous previous studies [16]. The fat distribution in women of reproductive age also has an impact on TTP. An increasing waist-hip ratio correlates with a reduced likelihood of conception per cycle [17]. The probability of pregnancy is reduced by 5% per unit in case of BMI over 29mg/m2 and the risk of infertility is three times higher in individuals with obesity compared to those with normal weight [10] .

2.6 Obesity and assisted reproductive technologies (ART)

Beyond natural conception, obesity complicates assisted reproductive technologies (ART). Multiple studies reported diminished outcomes of procedures like in vitro fertilization (IVF) of obese women compared to normal weight ones. Connection with embryo quality remains unclear [10]. The Kawwass et al. study reported that obese women had a lower absolute percentage chance of ART success. Both pregnancy and live birth percentage is lower among obese women in comparison to normal weight [18].

2.7 Possible interventions

Lifestyle modifications, particularly structured exercise and dietary adjustments, are highlighted as foundational to restoring metabolic balance and improving reproductive potential [9]. Clark et al. in prospective study examined if lifestyle modifications, including diet and exercise, may be considered a treatment option for infertility. Women who underwent

a 6 months program showed an increase in the number of ovulations, pregnancies, and live births [19].

Pharmacological treatments, such as metformin and GLP-1 agonists, may be successful in addressing insulin resistance and hormonal disruptions. Antioxidant supplementation and emerging therapies targeting adipokines further expand the possibilities of treatment. Bariatric surgery offers a pathway to significant weight loss and fertility restoration for severe cases, albeit with variable outcomes depending on individual factors [9].

3. General pathophysiology of woman infertility

Infertility, defined as the inability to conceive after at least 12 months of regular unprotected intercourse, affects approximately 10-15% of couples of reproductive age worldwide. The causes of female infertility include a variety of ovarian, tubal, and uterine factors, as well as conditions such as endometriosis, pelvic adhesions, and unexplained infertility. Each of these factors may act individually or in combination, leading to a complex pathophysiological picture [20,21].

3.1 Ovarian factors

3.1.1 Ovulation disorders

Ovulation disorders are one of the most common causes of infertility in women. These disorders can result from dysfunction of the hypothalamic-pituitary-ovarian (HPO) axis, hyperprolactinemia, thyroid dysfunction, or polycystic ovary syndrome (PCOS). Irregular pulsatile secretion of gonadotropin-releasing hormone (GnRH) disrupts the secretion of luteinizing hormone (LH) and follicle-stimulating hormone (FSH), leading to anovulation [20].

3.1.2 Low ovarian reserve

Ovarian reserve refers to the quantity and quality of remaining oocytes in a woman's ovaries. A natural decline in ovarian reserve with age is a common cause of reduced fertility in women over 35. However, some women experience diminished ovarian reserve earlier due to genetic factors, oncologic treatments, ovarian surgeries, or other conditions [20]. A low number and

quality of oocytes result in difficulty with fertilization and reduced developmental potential of embryos.

3.2 Tubal factor

The fallopian tubes play a crucial role in gamete transport, fertilization, and embryo migration to the uterus. Tubal damage is a significant cause of mechanical infertility, often resulting from pelvic inflammatory disease (PID), gynecological surgery, ectopic pregnancy, or endometriosis [20]. Tubal obstruction caused by adhesions or epithelial damage prevents the transport of oocytes and sperm, resulting in impaired fertilization or embryo implantation.

3.3 Uterine factor

3.3.1 Congenital anomalies

Congenital uterine anomalies, such as bicornuate uterus, unicornuate uterus, or the presence of a uterine septum, can lead to difficulties in embryo implantation, recurrent miscarriages, or preterm births. These anomalies primarily result from abnormal development of the Müllerian ducts during fetal life [21].

3.3.2 Acquired anomalies

Acquired uterine anomalies include uterine fibroids, endometrial polyps, and intrauterine adhesions (Asherman's syndrome). Submucosal fibroids and polyps may deform the uterine cavity, disrupting the implantation process. Intrauterine adhesions, which can develop after procedures such as uterine curettage, reduce the functional surface of the endometrium required for embryo implantation [20,21].

3.4 Endometriosis and pelvic adhesions

Endometriosis is a chronic condition in which endometrium-like tissue is found outside the uterus, causing adhesions and inflammatory changes in the pelvis. These adhesions may involve the fallopian tubes, ovaries, or other organs, disrupting their mechanical and hormonal functions. Endometriosis also affects the ovarian microenvironment, reducing the quality of oocytes and impairing embryo implantation [20].

Pelvic adhesions, which result from surgical interventions, infections, or endometriosis, can impair the transport of gametes and embryos, leading to mechanical infertility [21].

3.5 Unexplained infertility

Unexplained infertility is diagnosed in couples for whom no specific cause of infertility is identified despite thorough diagnostic evaluation. This condition accounts for approximately 15-30% of infertility cases. It is believed to result from subtle abnormalities in oocyte quality, embryo development, or endometrial microenvironment, which cannot be detected with standard diagnostic methods [20].

In unexplained infertility, immunological factors, such as the presence of anti-sperm antibodies or abnormal immune responses to the embryo, may play a significant role. Additionally, micro-changes in hormonal axis function, endometrial receptivity, or minor implantation defects might go undetected in routine medical examinations [21].

<table>
<tr><td colspan="4">Infertility</td></tr>
<tr><td colspan="2">General pathophysiology</td><td colspan="2">Obesity</td></tr>
<tr><td rowspan="5">Ovarian factors</td><td rowspan="2">Dysfunction of HPO axis</td><td colspan="2">Uncertain leptin effect</td></tr>
<tr><td colspan="2">Hyperestrogenemia caused by hyperandrogenemia leads to HPO axis disruption</td></tr>
<tr><td>PCOS</td><td colspan="2">PCOS and obesity comorbidity</td></tr>
<tr><td rowspan="2">Low quality of oocytes</td><td>Pro-inflammatory molecules</td><td rowspan="2">Oxidative stress may increase the risk of poor oocyte quality</td></tr>
<tr><td>Lipid accumulation</td></tr>
<tr><td>Uterine factor</td><td>Disrupted embryo implantation</td><td colspan="2">The inflammation negatively affect the endometrial lining resulting in reduction of receptivity to embryo implantation</td></tr>
<tr><td>Endometriosis</td><td></td><td colspan="2">Oxidative stress is associated with endometriosis</td></tr>
</table>

Table 1. The table summarizes the correlation between obesity and known contributors to female infertility.

Conclusions

The global rise in obesity demands an integrative approach to managing its impact on female infertility. Obesity affects women's fertility on many levels such as ovulation disruption and endometrial lining leading to reduction of receptivity to embryo implantation. Adipose tissue produces adipokines and pro-inflammatory molecules. The former disrupt sexual maturation and fertility while the latter may increase the risk of poor oocyte quality. It is worth noting that obesity co-occur with PCOS. The negative impact of obesity on assisted reproductive technology outcomes is confirmed. There is a need for further research and multidisciplinary collaboration to enhance obesity's importance in reproductive health. Effective interventions, raising awareness of obesity's implications and prioritizing its impact on healthcare systems, may lead to significant progress in improving fertility outcomes and overall reproductive well-being for women worldwide.

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References:

1. Marinelli S, Napoletano G, Straccamore M, Basile G. Female obesity and infertility: outcomes and regulatory guidance. *Acta bio-medica : Atenei Parmensis*. 2022;93(4):e2022278. doi:10.23750/abm.v93i4.13466

2. Caballero B. Humans against Obesity: Who Will Win? *Advances in nutrition (Bethesda, Md)*. 2019;10(suppl_1):S4-S9. doi:10.1093/advances/nmy055

3. Safaei M, Sundararajan EA, Driss M, Boulila W, Shapi'i A. A systematic literature review on obesity: Understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. *Computers in biology and medicine*. 2021;136:104754. doi:10.1016/j.compbiomed.2021.104754

4. Broughton DE, Moley KH. Obesity and female infertility: potential mediators of obesity's impact. *Fertility and sterility*. 2017;107(4):840-847. doi:10.1016/j.fertnstert.2017.01.017

5. Gajewski P, Szczeklik A, editors. Internal Medicine of Szczeklik 2023. Kraków: Medycyna Praktyczna; 2023. Polish

6. https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight (Access: 21.12.2024)

7. Olszanecka-Glinianowicz M, Mazur A, Chudek J, et al. Obesity in Adults: Position Statement of Polish Association for the Study on Obesity, Polish Association of Endocrinology, Polish Association of Cardiodiabetology, Polish Psychiatric Association, Section of Metabolic and Bariatric Surgery of the Association of Polish Surgeons, and the College of Family Physicians in Poland. *Nutrients*. 2023;15(7). doi:10.3390/nu15071641

8. Ross R, Neeland IJ, Yamashita S, et al. Waist circumference as a vital sign in clinical practice: a Consensus Statement from the IAS and ICCR Working Group on Visceral Obesity. *Nature reviews Endocrinology*. 2020;16(3):177-189. doi:10.1038/s41574-019-0310-7

9. Zheng L, Yang L, Guo Z, Yao N, Zhang S, Pu P. Obesity and its impact on female reproductive health: unraveling the connections. *Frontiers in endocrinology*. 2023;14:1326546. doi:10.3389/fendo.2023.1326546

10. Dağ ZÖ, Dilbaz B. Impact of obesity on infertility in women. *Journal of the Turkish German Gynecological Association*. 2015;16(2):111-117. doi:10.5152/jtgga.2015.15232

11. Jungheim ES, Moley KH. Current knowledge of obesity's effects in the pre- and periconceptional periods and avenues for future research. *American journal of obstetrics and gynecology*. 2010;203(6):525-530. doi:10.1016/j.ajog.2010.06.043

12. Cena H, Chiovato L, Nappi RE. Obesity, Polycystic Ovary Syndrome, and Infertility: A New Avenue for GLP-1 Receptor Agonists. *The Journal of clinical endocrinology and metabolism*. 2020;105(8):e2695-709. doi:10.1210/clinem/dgaa285

13. Lee B, Shao J. Adiponectin and energy homeostasis. *Reviews in endocrine & metabolic disorders*. 2014;15(2):149-156. doi:10.1007/s11154-013-9283-3

14. Tamura H, Takasaki A, Miwa I, et al. Oxidative stress impairs oocyte quality and melatonin protects oocytes from free radical damage and improves fertilization rate. *Journal of pineal research*. 2008;44(3):280-287. doi:10.1111/j.1600-079X.2007.00524.x

15. Manna P, Jain SK. Obesity, Oxidative Stress, Adipose Tissue Dysfunction, and the Associated Health Risks: Causes and Therapeutic Strategies. *Metabolic syndrome and related disorders*. 2015;13(10):423-444. doi:10.1089/met.2015.0095

16. Wise LA, Rothman KJ, Mikkelsen EM, Sørensen HT, Riis A, Hatch EE. An internet-based prospective study of body size and time-to-pregnancy. *Human reproduction (Oxford, England)*. 2010;25(1):253-264. doi:10.1093/humrep/dep360

17. Zaadstra BM, Seidell JC, van Noord PA, et al. Fat and female fecundity: prospective study of effect of body fat distribution on conception rates. *BMJ (Clinical research ed)*. 1993;306(6876):484-487. doi:10.1136/bmj.306.6876.484

18. Kawwass JF, Kulkarni AD, Hipp HS, Crawford S, Kissin DM, Jamieson DJ. Extremities of body mass index and their association with pregnancy outcomes in women undergoing in vitro fertilization in the United States. *Fertility and sterility*. 2016;106(7):1742-1750. doi:10.1016/j.fertnstert.2016.08.028

19. Clark AM, Thornley B, Tomlinson L, Galletley C, Norman RJ. Weight loss in obese infertile women results in improvement in reproductive outcome for all forms of fertility treatment. *Human reproduction (Oxford, England)*. 1998;13(6):1502-1505. doi:10.1093/humrep/13.6.1502

20. Bręborowicz GH, editor. Obstetrics and Gynecology. Vol. 1–2. 3rd ed. Warsaw: PZWL Medical Publishing; 2020. Polish.

21. Polish Society of Reproductive Medicine and Embryology (PTMRiE), Polish Society of Gynecologists and Obstetricians (PTGP). Diagnostics and Treatment of Infertility – Recommendations. Ginekol Perinatol Prakt. 2018;3(3):112–140. Polish.