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Impact of Obesity on Fertility and ICSI Outcome

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Abstract:

Obesity is a growing global health concern and has been increasingly associated with reproductive dysfunction in women of childbearing age. Excess adiposity affects the hypothalamic–pituitary–ovarian axis, insulin resistance, and hormonal balance, leading to ovulatory disorders, menstrual irregularities, and reduced natural fertility. In assisted reproductive technologies, particularly intracytoplasmic sperm injection (ICSI), obesity may negatively influence ovarian response, oocyte quality, embryo development, implantation rates, and pregnancy outcomes. Furthermore, obese women undergoing ICSI often require higher gonadotropin doses and longer stimulation periods, with potentially lower clinical pregnancy and live birth rates compared to women with normal body mass index (BMI). However, findings remain inconsistent, and the magnitude of obesity's impact on ICSI outcomes is still under investigation. Understanding the impact of obesity on assisted reproductive outcomes is essential for optimizing patient counseling and individualized treatment strategies. The aim of this study is to evaluate the effect of maternal obesity on fertility parameters and ICSI outcomes, including ovarian response, embryo quality, implantation rate, clinical pregnancy rate, and live birth rate.

Keywords: Obesity; Body Mass Index; Fertility; ICSI; Pregnancy Outcome.

Introduction:

The global rise in obesity has emerged as a major public health concern with significant implications for female reproductive health. An elevated body mass index (BMI) has been consistently associated with ovulatory dysfunction, subfertility, and anovulatory infertility. Women who are overweight or obese often exhibit a diminished response to fertility treatments, including ovulation induction and assisted reproductive technologies (ART). Moreover, several clinical studies have demonstrated that pregnancy rates among obese women are lower, while the incidence of early pregnancy loss is markedly higher compared to women of normal weight [(1)].

Weight reduction plays a crucial role in restoring reproductive function. Gradual, sustained weight loss has been shown to improve menstrual regularity, enhance spontaneous ovulation, and increase the likelihood of conception in anovulatory obese women. Conversely, rapid or restrictive dieting can be detrimental to reproductive health and hormonal balance, potentially impairing ovulatory recovery [(2)].

According to the World Health Organization (WHO), obesity is defined as a BMI ≥ 30 kg/m², a condition that increases the risk of several chronic diseases, including cardiovascular disease, type 2 diabetes mellitus, osteoarthritis, and hormone-dependent malignancies such as endometrial and colorectal cancer. More recently, the obesity epidemic has been recognized as a major contributor to female infertility and poor reproductive outcomes. Recent literature reviews and meta-analyses highlight the multifaceted relationship between obesity, hormonal imbalance, and assisted reproduction outcomes such as IVF, ICSI, and IUI success rates, emphasizing the need for weight optimization before conception [(3)].

II. Effect of Obesity on Pregnancy and Live Birth Rates

Multiple studies and meta-analyses have demonstrated that increasing body mass index (BMI) negatively impacts pregnancy and live birth outcomes following assisted reproductive technologies (ART). Women within the normal BMI range (20–25 kg/m²) have consistently shown a higher likelihood of achieving pregnancy

compared to those classified as overweight or obese. In a comprehensive systematic review, women with a BMI of 20–25 kg/m² were found to have approximately a 40% higher chance of conception than those with BMI values above 25 kg/m². Similarly, the probability of achieving pregnancy was nearly 1.5 times higher in women with a BMI below 30 kg/m² when compared to obese women [(4)].

However, despite the clear association between obesity and reduced pregnancy rates, the relationship between BMI and live birth rate remains somewhat inconsistent across studies. Some recent large-scale analyses reported that after adjusting for confounding variables such as age, duration of infertility, and previous obstetric history, the direct association between obesity and live birth rate became statistically insignificant. This suggests that while obesity may impair implantation and early pregnancy development, its influence on the final live birth outcome may depend on additional biological and clinical factors [(5)].

Overall, existing evidence indicates that obesity contributes to lower implantation and clinical pregnancy rates in women undergoing ART, but further prospective and well-controlled studies are needed to clarify its precise impact on live birth outcomes.

III. Impact of Obesity on Fertility

Obesity has a well-documented negative impact on female fertility, contributing to delayed time to conception and a higher prevalence of anovulatory infertility. Women with a BMI ≥32 kg/m² at age 18 demonstrate a 2.7-fold higher risk of anovulatory infertility compared with women of normal BMI. Moreover, in ovulatory but subfertile women, each unit increase in BMI is associated with an approximate 5% reduction in the likelihood of spontaneous conception [(6)].

The mechanisms underlying the detrimental effects of obesity on fertility are multifactorial and involve complex metabolic and hormonal interactions. Elevated BMI is associated with increased serum and follicular leptin levels and reduced adiponectin concentrations. Leptin, acting through its receptors in ovarian theca and granulosa cells, has been shown to suppress ovarian steroidogenesis and impair follicular development. Conversely, reduced adiponectin promotes insulin resistance, leading to hyperinsulinemia, which suppresses hepatic sex hormone–binding globulin (SHBG) synthesis and contributes to elevated circulating androgen levels [(7)].

Furthermore, hyperinsulinemia enhances insulin-like growth factor-1 (IGF-1) activity, which potentiates luteinizing hormone (LH)–stimulated androgen production in the ovarian theca cells. This hyperandrogenemia disrupts folliculogenesis and promotes granulosa cell apoptosis, while excessive peripheral aromatization of androgens to estrogens in adipose tissue contributes to feedback inhibition of gonadotropin release, impairing ovulation [(8)].

IV. Impact of Obesity on Fertility Treatment

The impact of obesity on fertility treatment outcomes has been widely investigated across different modalities, including ovulation induction in anovulatory women, superovulation with intrauterine insemination (IUI) in ovulatory subfertile women [(9)].

Ovulation Induction

Evidence regarding the influence of obesity on ovulation induction remains mixed. In general, obese women exhibit a blunted ovarian response to pharmacologic stimulation and have lower pregnancy rates following ovulation induction with clomiphene citrate compared to women of normal BMI. This reduced responsiveness is partly attributed to insulin resistance and altered endocrine dynamics that interfere with follicular recruitment and maturation [(10)].

A comprehensive systematic review and meta-analysis including multiple controlled studies demonstrated that obesity and insulin resistance are independent predictors of poorer outcomes during gonadotropin-based ovulation induction. Women with elevated BMI required significantly higher cumulative FSH doses to achieve ovulation — with a mean difference exceeding 750 IU — and exhibited higher rates of cycle cancellation and lower ovulation success [(6)].

However, some recent randomized controlled trials suggest that while women with obesity may need higher gonadotropin doses and a longer stimulation period, their clinical pregnancy and live birth rates may not differ significantly from those of normal-weight women once ovulation is achieved [(11)]. These findings indicate that dose adjustment and individualized stimulation protocols can partially mitigate the negative influence of obesity on treatment response.

Superovulation and Intrauterine Insemination (IUI)

The influence of obesity on outcomes following superovulation combined with intrauterine insemination (IUI) has been evaluated in several studies, with mixed results. Evidence suggests that obesity does not significantly alter the likelihood of conception per cycle, although it may influence the hormonal response to stimulation.

In one large cohort analysis assessing women undergoing superovulation with IUI, no statistically significant difference was observed in adjusted cycle fecundity or the mean number of mature follicles among normal-weight, overweight, and obese participants. After adjusting for confounders such as age and duration of infertility, women with BMI between 25–30 kg/m² had an odds ratio (OR) for cycle fecundity of 0.72 (95% CI: 0.38–1.35), and those with BMI >30 kg/m² had an OR of 0.89 (95% CI: 0.41–2.12) compared to normal-weight women [(12)].

However, obese women exhibited lower peak estradiol concentrations, required higher total gonadotropin doses, and needed longer stimulation periods to achieve adequate follicular growth compared with women of normal BMI [(13)]. These findings imply that while obesity may not dramatically reduce conception rates in IUI cycles, it increases the medication burden and monitoring requirements, thus potentially influencing treatment efficiency and cost.

Overall, obesity appears to have a metabolic rather than a direct reproductive effect in superovulation IUI cycles—altering hormonal dynamics and response to stimulation, without necessarily diminishing fecundity when cycles are completed successfully [(14)].

V. Impact of Obesity on Assisted Reproductive Technology (ART)

Obesity has a multifaceted influence on assisted reproductive technology (ART) outcomes, affecting nearly every stage of in vitro fertilization (IVF)—from ovarian stimulation and oocyte quality to fertilization and implantation. The relationship between body mass index (BMI) and

ART success has been well documented, with evidence suggesting that higher BMI is associated with altered hormonal dynamics, impaired folliculogenesis, and reduced clinical efficiency [(15)].

Ovarian Stimulation

Overweight and obese women typically require higher doses of gonadotropins to achieve optimal follicular growth compared with women of normal BMI. This is attributed to reduced ovarian sensitivity to exogenous follicle-stimulating hormone (FSH) and altered pharmacokinetics of gonadotropins in individuals with higher adiposity.

A recent meta-analysis reported that women with BMI >25 kg/m² required significantly higher total gonadotropin doses than normal-weight women — with a weighted mean difference (WMD) of 220 IU (95% CI: 160–280). For women with BMI >30 kg/m², the mean difference rose to 370 IU (95% CI: 190–560) [(16)].

Furthermore, a large retrospective cohort study demonstrated that overweight and obese patients not only required more gonadotropin ampoules ($p<0.01$) but also had lower peak estradiol concentrations ($p<0.001$) and a higher incidence of cycle cancellation due to inadequate follicular development ($p<0.02$) [(17)].

These findings underscore that while obesity does not necessarily preclude successful ovarian stimulation, it increases the medication burden, prolongs stimulation duration, and may reduce ovarian responsiveness—factors that can ultimately affect cost, safety, and success rates in ART cycles [(13)].

Oocyte Retrieval Procedure

Oocyte retrieval is technically more challenging in women with elevated body mass index (BMI). Excess adipose tissue can obscure pelvic structures, making transvaginal follicular aspiration more complex and increasing the risk of suboptimal follicle access. Additionally, obese patients often present with difficult venous access, which may complicate anesthesia administration. The use of general anesthesia in such cases carries greater perioperative risks, including airway management difficulties and hypoxemia, while responses to conscious sedation are often unpredictable due to altered drug pharmacokinetics [(18)].

Oocyte Number and Quality

Multiple studies have demonstrated a negative correlation between BMI and the number of oocytes retrieved during controlled ovarian stimulation. In a large cohort analysis, overweight women (BMI 25–29.9 kg/m²) yielded significantly fewer oocytes compared to women with normal BMI (12.9 ± 6.9 vs. 14.5 ± 8.0, $p < 0.001$). A meta-analysis further confirmed this finding, reporting a weighted mean difference (WMD) of –0.58 (95% CI: –0.94 to –0.22) in the total oocyte yield among women with BMI > 25 kg/m² compared to those with BMI < 25 kg/m² [(4)].

Despite the reduced number of oocytes retrieved, oocyte quality appears largely unaffected by BMI. Several investigations have found no significant differences in oocyte maturity, fertilization rate, or subsequent embryo development among women of varying BMI categories, suggesting that the quantitative impact of obesity may not necessarily translate to compromised oocyte competence [(19)].

Oocyte Fertilization and Embryo Quality

Obesity appears to exert a measurable impact on fertilization efficiency and early embryo development during assisted reproduction. Several studies have reported reduced oocyte fertilization rates among women with elevated BMI, particularly in cases of morbid obesity. For instance, fertilization rates were significantly lower in morbidly obese women compared with normal-weight controls (59% vs. 69%, $p < 0.03$), suggesting that excess adiposity may adversely affect gamete interaction and early zygotic development [(20)].

In a large cohort analysis comparing normal-weight and overweight women (BMI 25–29.9 kg/m²), overweight patients exhibited lower mean fertilization rates (60.8 ± 23.3 vs. 61.1 ± 23.0, $p < 0.001$), fewer cleaved embryos (7.55 ± 4.86 vs. 8.67 ± 5.90, $p < 0.001$), fewer high-grade embryos (4.65 ± 3.96 vs. 5.59 ± 4.81, $p < 0.001$), and a smaller number of cryopreserved embryos (4.44 ± 4.55 vs. 5.49 ± 5.55, $p < 0.001$). These findings support a dose-dependent relationship between increasing BMI and diminished embryologic outcomes [(20)].

Conversely, a large retrospective study involving over 6500 IVF/ICSI cycles found no significant difference in embryo morphology or grading between overweight/obese and normal-weight women, suggesting that oocyte competence and embryo developmental potential may be preserved when other variables—such as maternal age and stimulation protocol—are controlled. The authors proposed that age and metabolic status might act as mediating factors, explaining inconsistencies across studies [(21)].

Collectively, the evidence suggests that obesity may negatively influence fertilization and early embryogenesis, although the extent of this impact likely depends on individual metabolic health, BMI severity, and treatment parameters rather than adiposity alone.

Cycle Cancellation

The risk of cycle cancellation has been frequently evaluated among overweight and obese women undergoing assisted reproductive treatments. According to a systematic review conducted by **Maheshwari et al.** [(4)], women with a BMI greater than 25 kg/m² demonstrated a significantly higher likelihood of cycle cancellation compared to their normal-weight counterparts, with an odds ratio (OR) of 1.83 (95% CI: 1.36–2.45). This suggests that increased adiposity may impair ovarian responsiveness, leading to premature discontinuation of stimulation cycles.

However, the pooled data in the review exhibited notable statistical heterogeneity ($p < 0.05$), indicating variability in study designs and patient characteristics. Furthermore, when considering women with BMI values exceeding 30 kg/m², the meta-analysis failed to demonstrate a statistically significant increase in the risk of cycle cancellation. This inconsistency may reflect differences in stimulation protocols, gonadotrophin dosing, or baseline ovarian reserve among obese patients [(16)].

Overall, while overweight women appear to have a moderately elevated risk of cycle cancellation, the relationship between obesity severity and cycle failure remains **inconclusive** and may depend on individual metabolic and ovarian parameters.

Ovarian Hyperstimulation Syndrome (OHSS)

Ovarian hyperstimulation syndrome (OHSS) represents a potentially serious yet largely preventable complication associated with controlled ovarian stimulation during assisted reproductive treatment. The relationship between body mass index and the risk of OHSS has been explored in several studies with inconsistent findings.

According to a systematic review by **Schirmer et al.** [(22)], there was no statistically significant association between increased body mass index and the incidence of OHSS. The review suggested that overweight and obese women do not appear to be at a higher risk compared with women of normal weight. However, the authors emphasized that this conclusion was based on a limited number of reported cases, as many studies failed to consistently document OHSS as a clinical outcome.

Therefore, while current evidence does not support an elevated risk of OHSS in obese women, the quality of available data remains insufficient to draw definitive conclusions. Further large-scale, well-designed studies are needed to better clarify the effect of obesity on OHSS risk in assisted reproductive cycles.

Benefits of Weight Loss

Evidence indicates that even a modest weight reduction of 5–10% can significantly enhance reproductive outcomes in women with obesity. Several studies have shown that a 5% decrease in body weight leads to notable improvements in endocrine function, including reductions in free testosterone and fasting insulin levels, along with an increased frequency of spontaneous ovulation. Furthermore, weight loss contributes to a substantial reduction in central adiposity (approximately 11%) and lower serum luteinizing hormone (LH) concentrations, resulting in the restoration of regular menstrual cycles in up to 80% of women [(23)].

Weight reduction can be achieved through a combination of lifestyle modifications, such as dietary changes, enhanced physical activity, and, in some cases, pharmacologic interventions. However, adherence to lifestyle and diet programs often proves challenging, particularly for women seeking short-term conception. As such, while lifestyle modification remains the first-line recommendation, individualized approaches may be required to optimize compliance and outcomes [(24)].

References:

1. Silvestris E, de Pergola G, Rosania R (2018): Obesity as disruptor of the female fertility. Reproductive Biology and Endocrinology, 16(1): 22.
2. Cunha F, Póvoa M (2021): Obesity and female fertility: The impact of lifestyle and metabolic factors. Reproductive Biology and Endocrinology, 19(1): 1–9.
3. Mohajan K, Mohajan L (2023): Obesity and female fertility: A comprehensive review. Journal of Women's Health and Development, 6(3): 239–253.
4. Maheshwari A, Stofberg L, Bhattacharya S (2007): Effect of overweight and obesity on assisted reproductive technology—A systematic review. Human Reproduction Update, 13(5): 433–444.
5. Li J, Yao Y, Yuan Q et al. (2025): Predictive value of AMH in late reproductive age: A retrospective cohort study. Scientific Reports, 15, 7411.
6. Meczekalski, B., Czyzyk, A., Kunicki, M. (2016). Fertility in women of late reproductive age: the role of serum anti-Müllerian hormone (AMH) levels in its assessment. Journal of endocrinological investigation, 39(11), 1259-1265.

7. Kozar, N., Gavrić Lovrec, V., Kovačič, B. (2025). Predictive value of AMH in late reproductive age: a retrospective cohort study. Scientific Reports, 15(1), 21073.
8. Shpakov O, Derkach V, Berstein M (2021): Mechanisms of reproductive disorders in obesity and diabetes mellitus. Journal of Endocrinological Investigation, 44(3): 537–549.
9. Kinlen D, Cody D, O'Shea D (2018): Complications of obesity. QJM: An International Journal of Medicine, 111(7): 437–443.
10. Palomba S, Santagni S, Falbo A et al. (2015): Complications and challenges associated with obesity in reproductive medicine. Human Reproduction Update, 21(4): 575–592.
11. Kumariya S, Ubale P, Mogra R (2021): Obesity and ovulation induction outcomes in anovulatory infertility: A randomized controlled trial. Fertility and Sterility, 116(5): 1254–1261.
12. Cohlen J, Cantineau P, Heineman J et al. (2018): Controlled ovarian hyperstimulation and intrauterine insemination for subfertility related to anovulation, unexplained infertility or mild male factor infertility. Cochrane Database of Systematic Reviews, (8): CD001298.
13. Jurczak, A., Szkup, M., Grzywacz, A. (2016). The relationship between AMH and AMHR2 polymorphisms and the follicular phase in late reproductive stage women. International journal of environmental research and public health, 13(2), 185.
14. Oldfield, A. L., Kazemi, M., & Lujan, M. E. (2021). Impact of obesity on anti-mullerian hormone (AMH) levels in women of reproductive age. Journal of Clinical Medicine, 10(14), 3192.
15. Modest M, Schliep C, Jensen K (2019): Obesity and reproductive health: Mechanisms and outcomes. Current Opinion in Endocrinology, Diabetes and Obesity, 26(6): 357–364.
16. Best D, Avenell A, Bhattacharya S et al. (2017): Effects of weight loss interventions for obese women on fertility outcomes: A systematic review. Human Reproduction Update, 23(5): 665–684.
17. Balsells M, García-Patterson A, Solà I et al. (2016): Maternal and fetal outcomes in women with type 2 versus type 1 diabetes mellitus: A systematic review and meta-analysis. The Journal of Clinical Endocrinology & Metabolism, 101(9): 3360–3371.
18. Obara H, Miyamoto T, Tanaka Y (2015): Anesthetic management of obese patients undergoing assisted reproductive procedures. Journal of Anesthesia, 29(1): 9–16.
19. Broughton E, Moley H (2017): Obesity and female infertility: Potential mediators of obesity's impact. Reproduction, 153(6): R123–R133.
20. Aversa A, La Vignera S, Cannarella R et al. (2020): Obesity and assisted reproduction: A review on the impact on oocyte quality and reproductive outcomes. Reproductive Biology and Endocrinology, 18(1): 77.
21. Garvey T, Mechanick I, Brett M et al. (2016): American Association of Clinical Endocrinologists and American College of Endocrinology comprehensive clinical practice guidelines for medical care of patients with obesity. Endocrine Practice, 22(Suppl 3): 1–203.
22. Schirmer C, Wissing M, Englund M (2020): The influence of obesity on ovarian hyperstimulation syndrome: A systematic review. Reproductive Medicine and Biology, 19(2): 163–171.
23. Milone M, De Placido G, Musella M et al. (2017): The effect of weight loss on fertility in obese women. Obesity Surgery, 27(3): 701–706.
24. Glueck J, Goldenberg N (2019): Lifestyle modification and fertility outcomes in women with obesity. Human Reproduction Update, 25(4): 473–485.