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REVIEW

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Update on obesity and assisted reproductive technology

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Abstract

Background The effect of obesity on IVF consequences is still debatable.

Main body Obesity is linked to a greater likelihood of maternal and fetal complications all through gestation, including miscarriage, premature births, fetal demise, and adverse pregnancy outcomes. There was no increase in chromosomal abnormality percentages with increasing body mass index (BMI), implying that poor oocyte "performance" in obese patients could be caused by variables other than chromosomal expertise. Ribonucleic acid (RNA)-sequence research showed molecular changes in the oocytes of obese patients. Each 5-unit rise in female BMI is attributed with both a 5% and 7% reduction in hazard for CPR and LBR, in both, and a 9% rise in the comparative chance of miscarriage. There is no clinical or moral mandate for establishing a societal BMI limit for rejecting a client or couple direct exposure to infertility treatment. Assessment with an interdisciplinary approach prior to an IVF treatment should be done to assess the safety of oocyte retrieval under anesthesia, taking into account variables including body mass index and comorbid conditions. On LBR, there is no convincing evidence of the significance of lifestyle modification for losing weight. There is contradictory information on the impacts of weight loss surgery on pregnancy outcomes. IVF success rate was unaffected by weight loss surgery.

Conclusion Obesity has been linked to anovulation, decreased ovarian response to ovulatory prescription medications, changed oocyte and endometrial activity, an elevated risk of fertility problems, and reduced rates of live birth following IVF.

Background

Obesity is an international epidemic problem with a growing incidence [1]. Significantly, obesity was much more common in women than in men [2]. Overweight women with BMI 25.00–29.99 kg/m^2 accounted for 25% of reproductive-aged women, while obese women (BMI ≥ 30.00 kg/m^2) accounted for 23% [3].

The effect of obesity on IVF consequences is still debatable. Obesity has been linked to anovulation, decreased ovarian attentiveness to ovulatory prescription medications, altered oocyte and myometrial activity, an elevated risk of fertility problems, and lower rates of birth following IVF [4]. Moreover, there is an elevated likelihood of maternal and fetal complications during pregnancy, including spontaneous abortion, preterm delivery, fetal demise, and adverse pregnancy outcomes [5].

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Obesity's influence on embryo

1. Bellver et al. stated that obese and normal-weight women have the same embryo morphokinetic progression, blastocyst forming incidence, and blastocyst morphological characteristics [6]. On the contrary side, García-Ferreyra et al. revealed that a higher BMI impacts cell growth and decreases childbirth, implantation rate, and LBR [7]. Oocyte and embryo quality assessed according to classic morphological static parameters does not seem to be affected by excessive female body weight. However,

some metabolomic differences have been described in oocytes and embryos from obese women, thus pointing to a functional alteration.
2. Goldman et al. found no raise in aneuploidy percentages with increasing BMI, implying that poor oocyte "performance" in obese patients could be caused by variables other than chromosomal expertise [8]. The number or percentage of aneuploid, mosaic, or euploid fetuses was not really related to BMI [9].
3. Lipotoxicity boosted the concentrations of proinflammatory cytokines in the circulatory system, resulting in inflammatory responses in target tissues [10]. Follicular fluid metabolomics are changed in a wide range of ways in obese women [11]. RNA-seq studies have revealed molecular changes in the oocytes of obese patients [12].

Obesity's influence on the endometrium

A significant rise in euploid miscarriage in obese women implies that endometrial variables are involved in weaker IVF consequences in obese women. A greater body mass index (BMI) is linked to a decreased fertilization possibility [13]. There is really growing recognition of deficient embryo implantation in obese IVF patient populations [14]. The use of functional genomics analysis methods to investigate endometrial gene expression profiles revealed derangements of genes that encode cytokines and immune cells during the implantation window in obese women. Obesity has been linked to endoplasmic reticulum stress and mitochondrial dysfunction at the organelle stage [15].

Main text

Body mass index's influence on ART findings

The effect of obesity on IVF outcome measures is still questionable. Initial findings indicated that there was no link between BMI and IVF achievement [16], and yet two previous meta-analyses stated that increased BMI was linked to greater MR and lower CPR and LBR [17, 18]. Such research findings used unadjusted estimates, irrespective of the fact that female age, ET strategic plan (fresh and frozen ET protocols), and polycystic ovary syndrome are well-known variables involved for IVF end results. As a consequence, it is plausible that the observed effect of BMI was caused by these confounding variables.

Obesity has a negative impact on IVF outcomes

BMI and miscarriage after IVF

In both natural and ART, MR is risen in overweight and obese women [6]. The performance of oocytes and embryos as measured by classic morphometric static variables does not appear to be influenced by inordinate female body weight. Even so, some metabolomic variations in oocytes and embryos from obese women have also been characterized, indicating a fully functioning change.

As a result, the greater pregnancy loss percentage after IVF could be due to metabolomic, epigenetic, or mitochondrial oocyte and embryo disruptions or to the unusual endocrine, metabolic, and inflammatory uterine surroundings caused by overweight, which appears to be also willing to take responsibility for those other countless complications of pregnancy and the in utero fetal programming of postnatal chronic conditions.

A shift in the window of implantation has recently been documented in obese women undergoing artificial endometrial preparation, which could be linked to the lower embryo implantation rates and higher risk of miscarriage seen after fresh and FET with autologous oocytes, as well as with agreed to donate ova in receivers with incredibly high BMI. Obesity elevates the likelihood of miscarriage in cycles with frozen-thawed single blastocyst transfer but has no impact on the possibility of childbirth or a healthy baby [19].

Body mass index and live birth rate after IVF

Romanski et al. found no statistically significant variations in PR all over BMI categories [20]. Nevertheless, raising BMI was linked to a lower LBR in women who birthed via IVF/ICSI because of a higher percentage of pregnancy loss (12.6% in normal-weight women versus 22.2% in those with a BMI $40 \geq kg/m^2$). Miscarriage rate rises because of reduced endometrial receptivity, lowered oocyte quality, or even both. The number of retrieved oocytes, fully grown oocytes, zygotes, and cryopreserved blastocysts decreases with increasing BMI.

Live birth rate (LBR) was statistically significantly lower (RR = 0.85) in obese women undergoing IVF versus normal-weight women [18]. This could be thought to be due to a synergy of reduced CPR and greater MR, with the aforementioned becoming direct and the latter exacerbating the situation. In the overall assessment, a nonlinear relationship is noted with a higher likelihood of negative IVF consequences beyond a BMI of 30; however, most marked above a BMI of 35. Women considering IVF must be advised about the adverse effects of morbid obesity on IVF results. BMI and CLBR have an "inverted U shape" relationship [21]. The CLBR rises in underweight women, levels off in normal and overweight women, and afterwards falls in obese women.

Impact of obesity on the success of IVF

Upon frozen-thawed blastocyst transfer, LBR did not vary proportionally among obese and normal-weight patient populations [22]. Body's normal weight, overweight,

class I obesity, class II obesity, and class III obesity all had the same PR: 34.6%, 34.5%, 30.7%, and 41.7%, respectively. Sudden abortion in the second trimester is 2.13% and 1.35% in obesity classes I, II, and III [23]. A causal connection study of the link between PR and its consequences and BMI was not really demonstrated.

Even though maternal obesity increases the likelihood of very low birth weight infants by a small but significant amount, most embryology and pregnancy rates are comparable to normal-weight patient populations [24]. Fertilization, euploidy, MR, IR, and LBR were all equal between all women. There was no clear link for MR in donor oocyte cycles, which could be contributed to a variety of variables such as endometrial effect and baseline variances [25]. Because the subgroup assessment was predicated on research findings with minimal evidence, the findings must be taken with cautiousness.

Body mass index has no effect on donor oocyte recipient achievement [26]. In gestational carriers, CPR, LPR, and MR were not considerably different throughout the BMI categories [27]. Shown above research results are provisional and should be cautiously taken into account due to the low number of people involved with extreme obesity in the study results.

A pooled examination of two studies discovered a non-significant decrease in the hazard ratio of clinical childbirth when FET was used. Prior research has suggested that using FETs, which enable embryo transmission into more physiological uterine surroundings, could maximize the opportunities of IVF achievement [28]. Even so, the majority of research findings involve fresh cycle data, with very little information on FET accessible to investigate the impact of BMI on pregnancy outcomes.

The reality that BMI was classified as overweight, normal, or obese in their assessment limits extrapolation from such research findings [29]. A model with random effects was used in a meta-analysis to measure the RR for CPR, LBR, and MR after IVF. There were 18 cohort-based research totaling 975,889 cycles. Every 5-unit increase in BMI reduces the chances of CPR and LBR by 5% and 7%, respectively, and adds 9% to the comparative likelihood of miscarriage.

There is a non-linear relationship among BMI and CPR (non-linearity 105), with CPR falling steeply in obese women (BMI > 30). LBR has a fairly flat curve across a wide range of BMI from 16 to 30 (non-linearity = 0.0009). A J-shaped relationship among BMI and MR was noted, with a BMI of 22–25 resulting in the least miscarriage threat. Obesity enhanced the risk of negative IVF consequences in a non-linear dose–response way. Though the current study found a miscarriage rate threshold around a BMI of 22–25, the detailed mechanism underlying connections among overweight and IVF consequences remains unknown.

Management

Treatment recommendations: According to ASRM, there will be no clinical or ethical mandate for a societal-wide BMI threshold in 2021 [4]. There is a substantial body of evidence making the argument against such a strategy. Obesity alone cannot be used to reject a patient or couple access to infertility treatment. Personal programs should indeed be given the authority to perform oocyte retrievals and other processes in a safe manner. When obesity raises health consequences, an able to share decision-making procedures should be initiated, trying to balance patient's autonomy with normal efficiency.

Lines of treatment

1. Obesity-related fertility and maternal–fetal implications are addressed in prenatal counseling [4].
2. Assessment with an interdisciplinary team prior to an IVF cycle to assess the safety of oocyte retrieval under anesthesia, taking into consideration factors such as BMI and chronic conditions.
3. Both lifestyle changes and therapeutic treatment have been shown to be beneficial in encouraging losing weight. Two randomized controlled trials of lifestyle modifications [30, 31] found no evidence of a beneficial impact of short-term weight loss on pregnant women or LBR improved performance after IVF. On LBR, there is no strong evidence of the valuation of lifestyle modification for losing weight. In obese women, lifestyle modification previous to IVF does not really enhance embryo utilization or cumulative live birth rate [32]. The issue for women undergoing IVF is a battle with period. The duration it takes to lose weight may not be beneficial in combating the problems of declining ovarian reserve.
4. Actions for weight loss: Once suggesting delaying conception for the reasons of losing weight, consideration needs to be given to the patient's wish and preparedness to weight loss, in addition to the great promise influence on the overall probability of success with the postponed medical intervention [4]. Weight reduction intervention strategies enhance the likelihood of unaided birth in anovulatory women with obesity. The losing weight approach has made ovulation frequency in anovulatory women with obesity in reply to ovarian stimulation. They have not, even so, been demonstrated to enhance the LBR. Losing weight initiatives in ovulatory women with obesity have not been found to enhance the likelihood of live birth after non-ART therapy or IVF. It is uncertain how this will affect maternal and fetal problems.

5. Contrary data on the consequences of bariatric surgery on fertility have indeed been posted. Bariatric surgery has already been proposed as an improved method to enhance IVF clinical outcomes in obese infertile women [33]. There are enhanced IVF findings after bariatric surgery in a pilot study of women who had already failed repeatedly ART. Although bariatric surgery is an important adjunct to lifestyle changes and therapeutic treatment for weight loss, childbirth in women should be postponed for 1 year [4]. According to a multi-center retrospective European study, bariatric surgery seemed to have no massive effect on IVF achievement [34]. Following the first IVF cycle, women with a history of bariatric surgery who already had experienced IVF had a CLBR similar to non-operated patients with a similar BMI.

Conclusions

Obesity has been linked to anovulation, decreased ovarian attentiveness to ovulatory prescription medications, modified oocyte and endometrial activity, an elevated risk of fertility problems, and reduced birth rates following IVF.

Abbreviations

BMI	Body mass index
IVF	In vitro fertilization
LBR	Life birth rate
CPR	Clinical pregnancy rate
CRP	C-reactive protein
ART	Assisted reproductive techniques
MR	Miscarriage rate
ET	Embryo transfer
PCOS	Polycystic ovary syndrome
FET	Frozen embryo transfer
ICSI	Intracytoplasmic sperm injection
CLBR	Cumulative life birth rate
IR	Implantation rate
RR	Relative risk
RCT	Randomized control trial

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