



Obesity: A Troublemaker in Female Fertility

Sonia Malik¹ and Kanika Chopra^{2*}

¹Senior resident, Department of Obstetrics & Gynecology, Lady Hardinge Medical College, India

²Associate Professor, Department of Obstetrics & Gynecology, Lady Hardinge Medical College, India

*Corresponding author: Kanika Chopra, Associate Professor, Department of Obstetrics & Gynecology, Lady Hardinge Medical College, New Delhi, India

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Abstract

Obesity is highly prevalent in the present population. It has negative consequences on female reproductive health leading to infertility and poor response to treatment of infertility. Numerous studies have highlighted the link between obesity and infertility and we in our review tried to summarize it. Treatment of obesity should be the initial aim in obese or overweight woman in reproductive age group aiming for pregnancy. It's the responsibility of the treating gynecologist to counsel these subsets of women regarding the importance of necessary diet regimens and exercise plans in order to ensure better reproductive as well as health outcomes. Multi-disciplinary approach in association with dietician, yoga specialists and surgeons in women who are candidates for bariatric surgery.

Keywords: Obesity; infertility; weight loss

Introduction

Worldwide obesity has nearly tripled since 1975 (Global obesity epidemic) [1]. Both overweight and obesity have detrimental influences on the functioning of the human body including reproductive system. Obesity exerts a negative influence on female fertility. Obese women may undergo perturbations of the hypothalamic pituitary ovarian axis leading to anovulation and infertility [2]. Women with BMI over 25 kg/m² may take a longer time to conceive than women with BMI < 25 kg/m². Overweight or obesity may also be associated with decreased pregnancy rates and higher miscarriage events [3]. Obese women have reduced fecundity even when eumenorrheic and demonstrate poor outcomes with in vitro fertilization techniques. Obesity appears to affect the oocyte quality by disrupting meiotic spindle formation and mitochondrial dynamics. Excess free fatty acids may have a toxic effect on reproductive tissues, leading to cellular damage and a low-grade chronic inflammatory state. Altered levels of adipokines, such as leptin, in the obese state can affect steroidogenesis and directly affect the developing embryo. The endometrium may also show

evidence of impaired stromal decidualization in obese women. Obese polycystic ovarian syndrome women may even demonstrate a more severe metabolic and reproductive phenotype [4].

The impact of obesity on reproductive function, especially ovulatory disorders, is also attributable to dysregulation of neuro-endocrine function and ovulatory homeostasis [5]. In obese women, gonadotropin secretion is affected due to increased peripheral aromatization of androgens to estrogens while the insulin resistance and hyperinsulinemia lead to hyperandrogenemia. Furthermore, the sex hormone-binding globulin (SHBG), growth hormone (GH), and insulin-like growth factor binding proteins (IGFBP) are decreased and leptin levels are increased. Thus, the neuro-regulation of the hypothalamic-pituitary-ovarian (HPO) axis may be severely deranged. Obesity is considered to be a chronic low-grade inflammatory state with higher circulating levels of CRP, leptin, TNF- α , and IL-6 and lower circulating levels of anti-inflammatory adipokine called adiponectin [6,7]. The tissues of the reproductive tract are not immune to the inflammatory

state. In cultured primary human trophoblasts, exposure to IL-6 stimulates fatty acid accumulation and subsequent lipotoxicity [8]. Inflammatory pathways are critically important in reproductive events such as follicle rupture at the time of ovulation and invasion of the trophoblast into the receptive endometrium.

The developing blastocyst produces adiponectin, IL-1, and IL-6 [9]. The altered inflammatory milieu in obese women likely exerts an influence on these processes. Higher serum levels of leptin in obese women correlates with higher levels of leptin in the follicular fluid which affects steroidogenic pathways in granulosa cells, decreasing estrogen and progesterone production in a dose-dependent manner [10,11]. Overweight and obese women have poor outcomes following fertility treatment as compared to normal weight women. They poorly respond to ovulation induction, require higher doses of gonadotropins and longer treatment courses for follicular development and ovulatory cycles. In addition, the oocyte yield is lower in obese women resulting in a higher rate of cycle cancellation [12]. Reduction of obesity, particularly abdominal obesity, is associated with improvements in reproductive functions. Hence, treatment of obesity should be the initial aim in obese infertile women before embarking on ovulation-induction drugs or assisted reproductive techniques. While various strategies for weight reduction, including diet, exercise, pharmacological and surgical intervention exist, lifestyle modification continues to be of paramount importance [13].

Weight loss has been shown to improve reproductive outcomes by ameliorating fertility, as well as by regularizing menstrual cycles and increasing the chance of spontaneous ovulation and conception in anovulatory overweight and obese women. Weight loss results in an increase in SHBG, reduction in testosterone, improved menstrual function, improvement in conception rate and reduction in miscarriage rate. As central adiposity is associated with menstrual disorders and infertility, abdominal fat loss is critical in restoring ovulation. Weight loss of 5-10% may definitely improve the fertility rates [14]. It helps by causing significant improvement of endocrine parameters, such as decrease in levels of free testosterone, luteinizing hormone and insulin. Weight loss is associated with improvement in ovulation frequency, regularization of the menstrual pattern, decrease in cycle cancellation rates, increase in number of embryos available for intrauterine transfer, reduction in the number of ART cycles required to achieve pregnancy and a significant decrease in miscarriage rates [15]. The prime issues are long-term compliance with these strategies and maintenance of weight loss. The NIH recommends a multifaceted approach to treating obesity [16]. It emphasizes the importance of achievable and sustainable goals, notably a combination of diet, physical activity and cognitive behavior therapy. The key component of diet should be calorie restriction rather than the composition of the diet itself. Dietary intervention in managing obesity should aim for gradual weight loss via reduced calorie consumption and increased physical activity, with the overall aim of energy expenditure exceeding energy intake.

Sensible eating plans, tailored to individual weight and current dietary and exercise patterns, increase the chances of sustained weight loss. Diets based on healthy eating principles have a better long-term outcome, which is important because weight-loss maintenance requires that changes in eating habits should be sustained for life [17]. Exercise increases insulin sensitivity both by acting directly on muscle metabolism and indirectly by assisting in weight management. Quality of life and cognitive variables are important elements to consider with respect to lasting positive results in the long-term treatment of obesity. Cognitive behavioral therapy (CBT) has been demonstrated to be the most preferred intervention for obesity among overweight individuals, and it is one of the most commonly used psychological approaches. Patients benefit greatly from CBT as it can help to improve psychological skills, enabling stimulus control and a reduction in the quantities of food consumed. Learning behavioral modification strategies such as taking time to savor food, chewing slowly, and attaining a greater awareness of the pleasure of food that is associated with taste can also assist in weight loss [18]. Cognition has an important role in the expression of feelings and behaviour. A more realistic and adaptive perspective is achieved as the individual learns how to detect and react to dysfunctional thoughts, promoting a better emotional state and more adaptive behaviour to one's environment [19].

Conclusion

Overweight and obese women need longer time to conceive and undoubtedly are at higher risk of infertility. Oligomenorrhea and alterations of menstrual cycles should primarily alert overweight and obese women on their potentially defective fertility. The impact of obesity on reproductive function, especially associated with ovulatory disorders, is mainly due to dysregulated neuroendocrine mechanisms. Treatment of obesity itself should be the initial aim in obese infertile women before embarking on ovulation-induction drugs or assisted reproductive techniques. Multifaceted approach to treating obesity emphasizes the importance of achievable and sustainable goals, notably a combination of diet, physical activity and cognitive behavior therapy.

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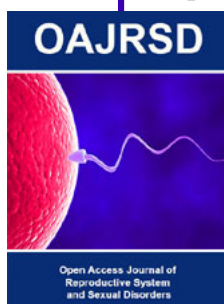
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