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## Research Article

# INFERTILITY AND OBESE WOMEN

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**ABSTRACT**

Obesity and overweight is not only anissue for developed countries, but also in the developing countries as well. Numerous studies have focused the link between obesity, infertility and adverse reproductive health outcome. Obesity plays a vital role in two most common medical risks in pregnancy: diabetes and hypertension. Weight loss has signified to improve fertility in obese women through recovery of spontaneous ovulation and better response to ovarian stimulation in infertility treatment. Therefore, for overweight and obese infertile women, weight management interventions should be appraised.



## INTRODUCTION

Obesity is a global health issue that has grown to epidemic proportions throughout the world. It is estimated that 1.3 billion people are overweight or obese globally (1). In the United States, between 2005–2006, data that 34% of U.S. adults of age 20 years and older -over 72 million people were obese.

Obesity was evaluated to contribute 8% of all illness costs (around £40 billion/year) (2). In pregnancy, the cost of prenatal care is 5 times higher for overweight women. In an another study carried out in Australian reported that 34% of the total samples of pregnant women were overweight or obese and they had increased adverse maternal and neonatal outcomes, resulting in increased costs of obstetric care (3). However, obesity is not only an issue of developed countries, but also in the developing countries as well (4-6).

Compared with normal-weight patients, obese women patients have a higher prevalence of infertility. They have elevated rate of early miscarriage and congenital anomalies. Obese women are more proneto have pregnancy-induced hypertension, gestational diabetes, thrombo-embolism, macrosomia, and spontaneous intrauterine death in the latter half of pregnancy (7). Obesity increases the risk of preeclampsia and fetal macrosomia and operative deliveries. Studies from different parts of India and Nigeria have provided evidence of the rising prevalence of obesity (8-12).

Obesity is a major contributing factor to the two most common medical risks in pregnancy: diabetes and hypertension (13-14). Although obesity is associated with an increased risk of large-for-gestational age, it is also associated with increased risk of hypertensive disorders, including preeclampsia, which may be linked with low birth weight (15). Obesity has also shown to be an independent risk factor for a longer, more laborious delivery and for a cesarean delivery (16-17).

### *Contributing Factors towards Obesity*

There are varieties of factors that play role in obesity. Overweight and obesity result from an energy imbalance that involves eating too many calories without energy expenditure. This imbalance can be a result of several factors which include individual behaviors, environmental and genetic factors.

### *Fertility and Possible Link with Obesity*

Nearly all obese women are not infertile; however, obesity and its negative impact upon fecundity and fertility are well observed. Obese women are 3 times more likely to suffer infertility than women with a normal body mass index (37). Obese women undergo impaired fecundity both in natural and

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assisted conception cycles (38). The mechanism through which its effect is exerted is more disputed.

Widely accepted mechanism to be involved in linking multiple metabolic abnormalities with obesity are hyperinsulinemia and insulin resistance. Such amendments involve androgens and oestrogens and their carrier protein, sex-hormone-binding-globulin (SHBG) (18).

Body fat distribution has been shown to substantially affect SHBG concentrations. Fat accumulation in the abdominal viscera has been reported as a possible cause of insulin resistance and the resulting metabolic syndrome. Women with central obesity and with higher proportion of visceral fat usually have high insulin resistance leading to lower SHBG concentrations in differentiation with those with peripheral obesity.

In insulin resistance syndrome, excess insulin is capable of stimulating steroidogenesis, excessive androgen production from the theca cells and excessive oestrogen production from the granulosa cells of the ovaries. In addition, by directly inhibiting SHBG synthesis, excess insulin may further rise the delivery of free androgens to target tissues. The excess in local ovarian steroidogenesis induced by excess circulating of insulin may cause premature follicular atresia and then favour anovulation.

Accumulating data conclude that insulin resistance and hyperinsulinemia resulting in hyperandrogenemia are the hormonal abnormalities, which disturb ovarian function in women with excess adipose tissue.

Fertility processes involves a complex factor and mechanism of both ovarian and extra ovarian origin. Obesity may interfere with many neuroendocrine and ovarian functions, thereby reducing both ovulation and fertility rates in otherwise healthy women. Oligo ovulation, anovulation and sub fertility are present in obese females with a relative risk of anovulatory infertility of 3.1 for women with a BMI >27 compared with women of BMI 20-25.

Polycystic ovary syndrome (PCOS), a major form of dysovulatory infertility in women, further complicates the issue (19). Many obese women have normal ovulatory menstrual cycles, remain fertile and have no apparent hyperandrogenism. Nevertheless, at the present time, there is substantial evidence to support the link between obesity and an ovulatory infertility (20). Particularly in obese women with PCOS, can result in many reproductive disorders. This results due to the complex interaction between the pituitary gland, pancreas and ovary resulting in a changed hormonal secretion pattern.

***Obesity and leptin***

Leptin, is a 16kDa messenger protein secreted by adipocytes-encoded by obesity gene protein. Leptin regulates body fat tissue by reducing food intake and increasing thermogenesis and, hence, weight of the body. Studies of its physiological action in humans have shown a +verelation between serum leptin concentrations and the percentage of body fat (22-24). Leptin levels have also been observed to be increased in women with PCOS, a major form of dysovulatory infertility in women, characterized by endocrine abnormalities such as hyperandrogenism and inappropriate LH secretion (25). Chakrabarti *et al*. attempts to evaluate the interrelationship between serum leptin level with body mass index, insulin and with circulating testosterone in PCOS women. He noted that hyperleptinemia in PCOS women appears to be due to the +ve relationship between serum leptin, BMI, and insulin (26).Given the well-established effect of leptin on ovarian steroidogenesis and ovulation in rodentsand in humans (27), it can be speculated that the high concentration of leptin might have a role in the pathogenesis of PCOS and reproductive disorders influenced by obesity.

***Obesity and menstrual disorder***

Oligomenorrhoea, amenorrhoea or irregular periods is often associated with obese women. Obese women had a rate of menstrual disturbance 3.1-fold more recurrent than women in the normal weight range. Teenage obesity was positively linked with abnormal, heavy menstrual flow and hirsutism later in life. Douchi T *et al*. carried out a study to find the contribution of upper and lower body obesity to obesity-related menstrual disorders and noted that obesity is associated with menstrual disorders (29).The existence of PCOS may further aggravate the effect of obesity on menstrual functions. Among the 1741 subjects with PCOS, 70% had menstrual disturbances and only 22% had normal menstrual function if their BMI was >30 kg/m$^2$) (30). Moreover, obese subjects with PCOS had an 88% chance of menstrual disturbance.

***Obesity, miscarriage and other adverse pregnancy outcomes***

Obesity is linked with an increased risk of miscarriage. Women weighing >82 kg are more probably to have miscarriage than thinner women as stated in a study carried out on primiparous women. In an another study carried out in women receiving donated oocytes also observed obesity as an independent risk factor for miscarriage (31).H. Lashen *et al*. assess the impact of obesity on the risk of miscarriage in the general public. The risks of early miscarriage and recurrent early miscarriages were significantly higher among the obese patients (odds ratios 1.2 and 3.5, 95% CI 1.01–1.46 and 1.03–12.01, respectively; $P$ = 0.04, for both] (32). High pre-pregnancy weight is linked with an increased risk of pregnancy-induced hypertension, toxemia, gestational diabetes, urinary infection, macrosomia, caesarean section, and increased hospitalization.

***Weight Management and Improved Reproductive Performance***

Many developments have been made so far on the effect of weight reduction in improving reproductive function in overweight and obese infertile women. It has been registered that weight reduction through dieting/exercising leads to improved reproductive performance. Weight loss is associated with significant improvement in reproductive function with reduction in hyperandrogenism, hyperinsulinemia and altered gonadotrophin pulsatile secretionas mentioned earlier in a study (33).Weight loss outcomesan increase in SHBG, reduction in testosterone and androgenicity, improved menstrual function, improved conception rates and depletion in miscarriage rates. Shick *et al*. carried out a cross sectional study to (34) assessed the dietary patterns of 438 subjects who maintained a weight loss of 30 kg for 5.1 years. individuals who successfully maintained weight notedcarried on consumption of a low energy and low fat diet. A systematic

evaluation of six randomized controlled trials using partial meal replacement plans for weight management suggests that these types of interventions can safely and effectively pro-duce significant sustainable weight loss and improve weight-related risk factors of disease (35). In addition to physical activity, behavior modification and healthy eating practices are essential. Clark *et al*. (36) carried out a study including a weight loss component to ascertain whether it could help infertile, overweight, anovulatory women. A weekly programme of behavioural change in relation to exercise and diet for 6 months resulted in an average weight loss of 6.3 kg, a restoration of ovulation in 12 of the 13 subjects and pregnancy in 11 women. Fasting insulin and testosterone concentrations fall significantly.

## CONCLUSION

The increase incidence of obesity reflects the profound changes in society and in behavioural patterns of subjects over recent years. Obesity causes abnormalities of sex hormones in women of reproductive age leading to oligo-ovulation, anovulation and subfertility. Furthermore, it is linked with increased risk of miscarriage, con-genital malformations, labor complications, neonatal morbidity and mortality. Treatments focused at reducing weight should represent the primary interventional policy in obese women with anovulation and infertility. Weight reduction is linked with better success rates in infertility treatment programmes. Therefore, weight reduction is the appropriate treatment for obese women with endocrine derangement, menstrual irregularities and infertility.

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