

OBESITY AND REPRODUCTIVE HEALTH By Steven C. Presser, M.D.

Reproductive health and infertility have gained much notoriety and public awareness has skyrocketed since the first test tube baby in 1978. (1) The same can be said about the impact lifestyle—namely the relationship between diet, exercise and heredity—may have on overall health risk. However, only recently in the medical community, and less so within the lay public, has an association been described between one's weight, nutritional status and reproductive health.

There appears to be a direct association between body weight and death from all causes between the ages of 30-55. When the BMI* exceeds 30, the relative risk of death, as relates to obesity, increases by 50%. Moreover, there are ethnic differences with a prevalence of increased obesity in African Americans, Hispanics and Caucasian females of 50.8, 40.1 & 30.6 respectively. (2)



Being overweight is associated with 400,000 deaths per year with significant increases in many health related disorders like cardiovascular disease, diabetes, hypertension and stroke, arthritis, fragile X syndrome, gout, sleep apnea, liver and gallbladder disease and colon cancer. (3,4) Additionally, overweight and/or obese (compared to normal weight) females have a greater incidence of reproductive-related disorders (Table 1), cancer of the breast, cervix, ovary and uterus, adverse pregnancy outcome and pregnancy-related disorders, (5,6,7) reproductive endocrinologic problems, infertility and urogynecologic disorders, to name a few. (8,9,10,11,12,13)

In that vein, although a thorough review of the literature describing the association between obesity and reproductive health is needed, the brief format of this communication doesn't lend itself to such an article. Therefore, the major areas will be highlighted and conclude with some recommendations.

Cancer

The incidence of certain types of cancer are significantly increased in the overweight population. (14,15) In women, those of the reproductive system are more common. Epidemiologic studies in the past suggested that populations whose diets were high in fat have an increased incidence in breast cancer. More recently, there not only appears to be a relationship between total body fat and breast cancer, but the increase in central (visceral) body fat assessed by CAT scan, may have a greater impact on the overall risk. (16)

Similarly, the risk of developing endometrial (uterine) cancer is also increased in overweight women, thought to be a consequence of an overproduction of estrogen by the adipose (fat) tissue cells. This increase in the estrogen production by the adipose tissue cells in the postmenopausal female is primarily related to the amount of excess body fat.

Obstetrical Outcome

A number of studies have shown the relationship between being overweight or obese and adverse obstetrical outcome. (17,18,19) A recent study of 2,459 Danish women, (5) divided into three groups based on their pre-pregnancy BMI: normal weight (BMI 18.5-24.9), overweight (BMI 25-29.9), obese (BMI>30) were evaluated in terms of their clinical obstetrical outcomes. After adjustments for other factors, both overweight and obese subjects were found to have significant increases in hypertensive complications, caesarian section, induction of labor and excessive fetal size for gestational age in the presence of a normal glucose tolerance. An associated by-product of the increased caesarian rate is the higher perioperative morbidity, including anesthetic difficulties, infection, problems with wound healing, blood loss and lengthy hospitalizations. Other studies have shown a direct relationship with an increased BMI of >30 & >40 both showing increased rates of gestational diabetes and pregnancy induced hypertension. (5,20)

Reproductive Performance & Endocrine Changes

There are a significant number of overweight and obese females who suffer infertility. This could be a consequence of irregular menses and frequently anovular cycles. (8,9) A large percentage of those infertile patients have Polycystic Ovarian Syndrome (PCOS), a disorder often associated with obesity, chronic anovulation, and menstrual irregularity with or without hyperandrogenism and hyperinsulinemia. (21) Anovulation is also seen in patients with a BMI > 30 due to abnormal secretion of hypothalamic GnRH, pituitary LH and FSH. (28) The hyperinsulinemia seen with an insulin resistant state without PCOS can impact on fertility independently. Although the exact mechanisms of how obesity affects fertility are not well understood, there is an apparent insulin-mediated hyperstimulation of ovarian steroid production and decreased sex hormone-binding globulin.

Obesity has also been associated with an increased risk of early pregnancy loss after IVF, decreased pregnancy rate, decreased fertilization, higher gonadotropins requirements, as well as an impaired response to gonadotropins. (22,23) The cause of a poor IVF treatment outcome may be due to poor oocyte quality with subsequent lower fertilization and/or implantation defects caused by a qualitatively poor endometrial milieu. Finally, there are a number of endocrine changes that are associated with being overweight or obese. (24) (Table 2)

Conclusions

The conventional approach in the past has been to carefully monitor patients who have high risk pregnancies; e.g. gestational diabetes, multiple gestations, etc. Based on more recent data, it seems that overweight/obese individuals represent another high risk group. Yet, widespread routine high risk screening of obese patients has not become the standard of care. Additionally, due to the greater incidence of clinical problems in the

infertile obese population, these patients should also be considered high risk and treated accordingly.

To that end point, our initial treatment of the infertile, overweight/obese patient should include a multidisciplinary approach to weight management that fosters lifestyle change through proper diet, exercise, behavior modification and stress reduction in concert with pharmacologic approaches (e.g. Metformin) when indicated. By providing a more holistic approach to obesity and reproductive health preconceptually, we may be able to have a powerful impact on our patients by enhancing their chances of conception, achieving a healthy obstetric outcome and possibly enhancing their overall health.

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*The BMI is a measure of your weight (in kilograms) relative to your height (in meters squared). BMI is a reliable indicator of body fat and when used with other information, can provide a risk of developing overweight/obesity-related diseases. One is considered overweight with a BMI>25, obese if >30 and severely obese if >40.

TABLE 1

ASSOCIATION BETWEEN OVERWEIGHT/OBESITY AND INCREASED INCIDENCE OF REPRODUCTIVE PROBLEMS

Birth Defects	Ovulatory Disorders
Cancer	Menstrual Disorders
Caesarian Section	Miscarriage Rates
Fertilization Rates	Number of Atretic Follicles
Gestational Diabetes	Pregnancy-Induced Hypertension
Hirsutism	Pregnancy Rates
Hyperandrogenism	Postoperative Wound Infection
Hyperinsulinemia	Polycystic Ovarian Syndrome
Impaired Response to Gonadotrophins	Urinary Stress Incontinence