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ROLE OF WEIGHT REDUCTION AND ITS SIGNIFICANCE IN RESTORING FERTILITY - IN OBESE AND OVERWEIGHT WOMEN

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ABSTRACT: OBJECTIVE: To assess the role of obesity (in terms of body mass index) on female fertility. **Methods-** A prospective study of 62 obese women over a period of 2 years from June 2009 to May 2011 at Calcutta National Medical College was done. **RESULTS:** Fertility regained in 25.72% after weight reduction. Estimated success probability equals 0.2592. P value was statistically significant. Weight reduction of 7-10kgs of body weight was achieved in 62.5% patients. **CONCLUSION:** Weight reduction is the appropriate treatment for women with obesity related infertility.

KEYWORDS: Body mass index (BMI), obesity, infertility.

INTRODUCTION: Obesity has become a worldwide epidemic with ever increasing incidence and public health problem in both developing and developed countries¹. In obese women, the rate of complications during pregnancy and delivery and the prevalence of gynecological tumors like endometrial or breast cancer is higher². Obesity is also associated with infertility and menstrual irregularity³. Recent data suggest that overweight and obese patients are also at increased risk of recurrent pregnancy loss (RPL) that affects 1% of the fertile population⁴. Obesity is measured by body mass index (BMI) which is the ratio of weight in kilogram divided by height in m². Approximately 1.6 billion adults worldwide are overweight (BMI 25-30 kg/m²) and at least 400 million were obese (BMI > 30kg/m²) in 2005. These figures are expected to rise to 2.3 billion and 700 million respectively, by 2015. The prevalence of obesity is relatively low in Asian countries with 4% of Chinese and 0.5% of Indian women noted to be obese⁵.

Obesity in women has shown to increase time to conception⁶. The relative risk of anovulatory infertility is 2.7 (95% CI, 2.0-3.7) in women with BMI $\geq$ 32kg/m² at age 18⁷. While in ovulatory but subfertile women the chance of spontaneous conception decreases by 5% for each units increase in the BMI⁸.

AIMS AND OBJECTIVES: This was a prospective study to investigate the relationship between weight reduction and its effect on fertility in obese / overweight women.

MATERIALS AND METHODS: A total of 62 obese female with body mass index > 25 kg/m² with menstrual dysfunction aged 20-45 years were selected for this study. Women who presented with infertility of 4.5 $\pm$ 3 years duration were included. The study was conducted for 2 years between June 2011 to May 2013 at Calcutta National Medical College and Hospital in the department of Obstetrics and Gynecology.

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Inclusion criteria: Obesity, infertility, menstrual irregularity without any thyroid and prolactin abnormality. In this group of 62 women, 7 had features of polycystic ovaries in pelvic ultrasonography.

After giving weight reduction treatment by dietary restriction and exercise, patients had been advised to report after 6 weeks in the outpatient department for follow up. The diet was restricted to only 1200 calories / day. Approximate 1200 calories intake was divided into 5 meal timings. An early morning snacks (60 calories), Breakfast (150 calories), Lunch (500 calories), an afternoon snack (120 calories) and Dinner (470 calories).

In every follow up visit history was taken to note any subjective improvement, clinical examination was done to note reduction in body mass index or only clinical improvement (positive pregnancy test).

RESULTS:

Age	No. of Patients	Percentage
20-25 yrs.	14	22.58%
25-35 yrs.	30	48.38%
35-45 yrs.	18	29.03%

Table I: Demographic Variation (n = 62)

Body Mass Index		
25-29.9 (overweight)	20	32.25
30 and above (obese)	42	67.74

Table II: Distribution of patients (n = 62) according to body mass index (kg/m²)

6 patients out of 62 obese patients did not follow the weight reduction treatment schedule. Rest 56 patients followed the treatment scheduled. The 6 patients who did not follow the treatment schedule, failed to show any clinical improvement regarding body mass index and fertility.

Fertility	No. of patient	%
Fertile	20	42.55
Primary infertility	12	22.53
Secondary infertility	15	31.91

Table III: Fertility status of the patient

Result of wt. reduction	No. of patient	%
BMI 30 and above	16	28.57
BMI 25-29.9 kg/m ²	15	26.78
BMI 20-25	25	44.64

Table IV: Effect of weight reduction schedule on body mass index (n = 56)

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16 patients with pretreatment body mass index 30 and above and 5 patients with pre-treatment body mass index 25-29.9 did not respond to treatment schedule and remained obese. Out of 56 patients who followed the weight reducing schedule, 35 (62.5%) patients reduced their weight with an average reduction of 7-10 kgs of body weight.

Number of patients to conceive after weight reduction schedule	Number of infertile patients	Percentage
7	27	25.75%

Table V: Number of patients regained fertility after weight reduction schedule

Fertility regained in 7 patients out of 27 infertile patients after weight reduction.

Estimated success probability is 0.2592. Estimated variant of success probability is 7.11×10^{-3} and the 95% confidence interval for P (0.094, 0.424 i.e. with 95% confidence we can say that p will lie between 0.094-0.424). The result is statistically significant.

Reduction of BMI after Rx	No of patient	Percentage (%)
Pretreatment BMI 30 and above reduced after treatment to BMI 25-29.9	2	28.57
Pretreatment BMI 30 and above reduced after treatment to BMI 20-25	4	57.14
Pretreatment BMI 25-29.9 reduced after treatment to BMI 20-25	1	14.28

Table VI: Distribution of patients who regained fertility after weight reduction (n=7) according to BMI

DISCUSSION: Obesity is an excess of body fat. It may be hypertrophic, hyperplastic or a combination of both. Fat cells or adipocytes have aromatase activity. Obese women have excess number of fat cells in which extraglandular aromatization of androgen to estrogen occurs. They also have lower circulating levels of Sex Hormone Binding Globulin (SHBG) which allows a large proportion of free androgen to be converted to estrone. Increased estrone triggers an increase in Luteinizing Hormone (LH) with consequent ovarian hyperstimulation, leading to increased testosterone and anovulatory cycles. The decrease in SHBG also allows an increase in free androgen levels.

Several studies show that weight reduction induced by exercise and low calorie diets improves hyperandrogenemia, insulin resistance, and menstrual dysfunction¹⁰. Many authors recommended weight loss as the best, cheapest and cause related therapy of infertile, obese women. Commonly these women do not respond easily to the usual treatment with antiestrogens and gonadotropins.

In our study, after weight reduction 25.72% of patients conceived subsequently. At the end of our study majority of the patients were still continuing their pregnancies and some had live births. Our study results are less when compared to Bates and Whitworth study with 77% pregnancy rates after weight reduction of 15% of body weight⁹. But has similar results like Hollmann et al study which showed 29% pregnancy rates¹⁰.

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Obese women often have a decreased reproductive potential, as evidenced by menstrual disturbances, anovulation, time to conception, poor response to ovulation induction and reduced pregnancy outcome¹¹. The imbalance in the estrogens and androgens cause irregular ovulation and anovulation. Obesity accounts for infertility 15-20% of infertile patients. A poor quality of ova even in presence of ovulation leads to subfertility. Obese women require higher doses of drugs and prolong treatment and still do not respond to fertility treatment satisfactorily.

The results of this study support the hypothesis that it is possible to improve fertility rates in obese or overweight women with lifestyle modification by using a lifestyle program that sets realistic weight loss and exercise goals. Subjects were able to sustain hormonal imbalances, menstrual irregularities and regain ovulation to achieve pregnancy. Weight loss in these subjects resulted in resumption of ovulation and correction of the hyperandrogenemia.

Abdominal obesity is associated with increased level of insulin, chronic hyperinsulinemia causes increased ovarian androgen production, increased LH secretion from pituitary and decreased sex hormone binding globulin production leading to increase in free circulating androgen, and this androgen becomes aromatized by fat cells to estrogen leading to chronic hyperestrogenic environment¹².

Even of 5% decrease in weight improves fertility in obese PCOS by decreasing fasting insulin levels and increased frequency of ovulation.

Norman RJ and Clark AM 13 during their study regarding obesity and reproductive disorder, found obesity has significant consequences for the reproductive system, depending upon the amount and distribution of body fat. Obesity contributes to menstrual disorders, infertility, miscarriage, poor pregnancy outcome, impaired fetal well-being and diabetes mellitus. Central adiposity is particularly important in clinical sequelae associated with an increased body mass index. They showed that weight loss has marked effects on improving the menstrual cycle and promoting spontaneous ovulation and fertility. Results indicate that fertility is improved through exercise and sensible eating pattern when conducted in a group environment. The mechanism is probably associated with changes in sensitivity to insulin¹⁴.

CONCLUSION: Obesity in women has impacts on fertility and fertility treatment. Increase in body mass index reduces the chance of conception in women. Obesity is associated with lower fertilization rates, poor quality embryos and higher miscarriage rates. Weight loss in these women improves their reproductive outcomes; however, in order for this to be effective it has to be gradual and sustained.

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