

**Obese women with polycystic ovary syndrome and Pregnancy: a case report and a literature review****Mania Amiri<sup>1</sup>, Masoumeh Golsorkhtabaramiri<sup>1,\*</sup>, Treza Mahouti<sup>1</sup>, Faeze Ghofrani<sup>1</sup>, Fateme Ashabi<sup>1</sup>, Fateme Nadi Heidari<sup>1</sup>, Somaye Azizi<sup>1</sup>**<sup>1</sup> Infertility and Reproductive Health Research Center, Health Research Institute & Clinical Research, PCOs clinic, Babol University of Medical Science, Babol Iran**Received: 6 Feb 2016      Accepted: 8 Mar 2016****Abstract**

Many women with polycystic ovary (PCO) are obese. These women have lower clinical pregnancy rates when compared with their lighter counterparts. We hereby present a case of an obese PCOs woman, who referred to our clinic, underwent a microinjection, and failed in pregnancy. Then, she was recommended to have a change of lifestyle and lose weight along taking insulin-sensitizer medicines. In the following 6 months, she lost 19 Kilograms and referred to us with a spontaneous pregnancy. The object of this report was to determine the role of insulin intolerance medicines and lifestyle improvement on enhancing the rate of pregnancy in the PCOs obese women.

**Keywords:** Life style, Obesity, Polycystic ovarian syndrome, Pregnancy, Weight Loss

**Introduction**

Obesity is reported to be associated with chronic anovulation in women (1). In patients undergoing Assisted Reproductive Technique (ART), the implantation, clinical pregnancy, and live birth are decreased by increasing the body mass index (BMI) (2, 3). Polycystic ovary syndrome (PCOs) is an endocrine disease, which may result in obesity. Research suggests that the co-occurrence of metabolic syndrome like insulin resistance and PCOs in women is regarded as a common etiology (4). In this case, we report how losing weight (by insulin sensitizer medicines and modification of life style), following a failed ART, helped an infertile woman with polycystic cystic ovary become pregnant. In addition, we reviewed the advantages of the quality of life and the effect of insulin sensitizer medicines as the co-treatment of infertility on PCOs phenotype women.

**Case report**

A 32-year-old woman, BMI >36, who had an approximately regular menstruation and a 6-year-history of primary infertility was admitted to our Infertility Center in Babol (north of Iran). She had no history of a particular disease.

In preliminary physical examination, including pelvic examination, the breast and thyroid were normal. Her husband's semen analysis was normal, too. In hormonal investigations (cycle day 2-4), the follicle-stimulating hormone (FSH) level was less than 10 mIU/mL, and the Prolactin (PRL) and thyroid stimulating hormone (TSH) level was also normal, but the luteinizing hormone (LH) level was elevated.

The size and the shape of uterus was assessed using hysterosalpingography (HSG), and the result was normal. In addition, a diagnostic laparoscopy was performed to assess the health of uterus, tubes and ovaries and also to look for any associated endometriosis and polycystic ovary (PCO).

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First of all, the patient was referred to the PCO clinic for changing her life style and losing weight, but due to her previous attempt to lose weight and the subsequent disappointment, she refused to do it and insisted on Intracytoplasmic Sperm Injection (ICSI). The advantages and the disadvantages of this method were thoroughly explained to the couple. In the initial ultrasound to start the ICSI, some echogen sites were seen in the uterus, and a repairing hysteroscopy was performed prior to ICSI. The pathology reported an endometrial polyp.

Then, the patient entered ICSI by the stimulation of ovulation, but at the time of occyte retrieval, she was involved with Ovarian Hyperstimulation syndrome (OHSS). Therefore, her fresh formed embryos were not transferred, and the patient entered the rest phase.

After a six-month delay, which was due to menstrual disorders, she referred to the center for the transfer of the frozen embryo. Two series of embryos were (2 embryo in each serious) transferred with a 3-month interval. The clinical pregnancies were negative in all series. Unfortunately, the patient entered the depression phase and needed to use anti-depressant medicine (sertraline 100 mg/day) and cognitive-behavior therapy (one day in a week) for 6 months. On her new admission, we strongly recommended the patient to refer to our PCOs clinic following the end of the psychology treatment and she accepted it.

At first, the blood sugar and the lipid profile of the patient were assessed. Fasting insulin (FINS) and fasting blood sugar (FBS) were elevated, while the glucose tolerance test (GTT) appeared in a normal limit. The offered treatment included the administration of metformin 500mg 2 tab/day and flutamid 250 mg 2 tab/day (As required) for 6 months to lessen the elevated FINS level associated with liver function monitoring. In addition, a standardized hypocaloric diet comprising 1200-1400 kcal/day, 50% carbohydrates, 30% proteins and 20% fat was initiated. The dietary energy composition was calculated by subtracting at least 500 kcal from the usual individual energy intake. The final composition of the diets ranged between 1200 and 1400 kcal /d (5). During the six-month period, she was not undergoing infertility treatment. She followed a moderate aerobic exercise and Behavioral education, and was given additional support. During the following 6 months, she lost 19 kilograms. In the seventh weeks, she came to the PCOs

center with the retardation of menstruation. The clinical pregnancy was positive and the pregnancy was confirmed with transvaginal ultrasonography. After a full-term pregnancy, a healthy baby was born.

## Discussion

Approximately, half of the women with PCOs are overweight or obese. They are involved with weight gain for more than ten years. The PCOs women have extended medical implications for the health of women. On the other hand, a greater prevalence of metabolic abnormalities is seen by the presence of obesity alongside PCOs phenotype (6, 7, 8). The women with PCOs are seven times more likely to be at the increased risk of enhancing type II diabetes and a 33% risk of impaired glucose tolerance, and up to 10% involve diabetes at a young age ( 8, 9, 10,11).

Many obese PCOs women are insulin resistant and hyperinsulinemic. Both insulin resistance and hyperinsulinemia cause body fat, probably diminishing spontaneous and induced ovulation in the obese PCOs women. The presence of insulin receptors in the ovarian tissue and the overproduction of androgens by theca cells tend to establish hyperandrogenaemia (12). As obesity in the abdominal phenotype may accelerate hyperandrogenism in the PCOs women, the sex hormone binding globulin (SHBG) serum declines and free androgens are delivered to peripheral tissues. On the other side, insulin seems to stimulate the sensitivity of pituitary gonadotropes to gonadotropin releasing hormone (GnRH), increases the ovarian steroidogenic response to gonadotropins, and increases the LH receptors (13, 14). In the presence of the reducing insulin levels, both hyperandrogenism and the related clinical features may enhance.

The role of obesity was clearly recognized in the case of hyperinsulinemia and insulin intolerance when the normal weight and the obese PCOs study groups were compared with each other. The obese PCOs women had a more severe insulin-resistant state when compared with their non-obese PCOs counterparts. In 95% of obese PCOs women, the glucose intolerance and also the defect in sugar metabolism chain was presented (15). There are studies (16, 17, 18, 19) indicating that obesity contributes an additional component to insulin resistance in obese PCOs.

Insulin sensitizing drugs such as metformin with few side effects were reported to have a long-term

safety data, and are inexpensive for PCOs patients. It lessens insulin intolerance, inhibits ovarian androgen production and also improves menstrual cycle in PCOs women (20, 21, 22).

Metformin, for instance, has proved to improve fertility in PCOs women (5, 23, 24). It can be used as a co-existent pre-diabetes, and diabetes mellitus even when lifestyle modification does not work (25). According to Toskani et al, insulin resistance is not associated with the amount or the quality of diet in PCOs women (26). For this reason, we administered metformin at the onset of hypocaloric diet as a weight loss component.

Weight loss through combining lifestyle modification with metformin as compared with metformin alone has many advocates (27). However, some studies indicated that metformin alone as compared with placebo had no effect on body mass index (BMI) values for PCOs women (28, 29).

Naderpoor et al. reported the effect of metformin on improving the lifestyle through weight management in women with PCOs (21). Lifestyle modification has been identified with reducing dietary fat intake to 25–30% of the total calories (30), cognitive behavioral therapy and exercise, which can all affect the weight loss process. Moran et al. in a review article confirmed the benefits of diet and exercise on weight loss and demonstrated that lifestyle could definitely help us lose weight (31).

Obesity is associated with unfavorable assisted reproductive technology (ART) outcomes in the PCOs patients, particularly in the case of repeated implantation failure (32, 33). These failures anticipate subsequent psychological distress (34, 35). In the case of our patient, the pregnancy failed even after two attempts of transferring frozen embryos, and she consequently experienced a period of depression. Hence, we had to refer her to our center of fertility stress management for psychological treatment.

Junguim et al. reported that obese women with PCOs have less mature oocytes retrieved, lower fertilization rates, lower clinical pregnancy rates and also lower delivery rates than those with a BMI  $\leq 39$  (36). Thus, given the impact of lifestyle on weight loss in our case, the quality of life in PCOs women should be regarded as a priority before proceeding with ART.

## Conclusion

Lifestyle improvement and the use of insulin sensitizer medicines for weight loss as two complementary options are recommended alongside ART.

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## Conflict of interest

None

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