

## Comparison of leptin concentrations between infertile women with polycystic ovary syndrome and fertile women

### Abstract

**Background:** Some studies propose that changes in leptin concentrations (above or under the normal range) result in infertility. Therefore, we investigated serum and follicular fluid leptin concentrations in infertile women with polycystic ovary syndrome (PCOS).

**Objective:** To study serum and follicular fluid leptin concentrations in infertile women with PCOS.

**Materials and Methods:** We conducted a case-control study. The case group consisted of 30 infertile women with PCOS who were admitted to the Infertility Department of Imam Khomayni Hospital in Ahvaz, Iran. The control group consisted of 30 healthy fertile women adjusted for age and body mass index (BMI) with the case group. On day 14 of the menstrual cycle, 5 ml of blood was obtained from subjects in both groups. Serum and follicular fluid leptin concentrations were determined by the enzyme linked immunosorbent assay (ELISA). A Biovendor kit was used for the measurement of leptin concentrations. All data were analyzed using statistical package for the social sciences (SPSS) software (version 17.0, Nie, Bent & Hull, USA).

**Results:** There was a significant correlation between BMI and serum leptin concentrations in both the control ( $p=0.005$ ,  $r=0.516$ ) and case groups ( $p=0.006$ ,  $r=0.547$ ). In the case group, serum leptin concentrations were consistent with follicular fluid leptin concentrations ( $p<0.001$ ,  $r=0.839$ ). Comparison of serum leptin concentrations between the case and control groups revealed no significant difference ( $p=0.56$ ).

**Conclusion:** Infertility among women with PCOS was not a consequence of changes in leptin concentrations.

**Keywords:** Polycystic ovary syndrome, Leptin, Infertility.

### Dear Editor

Infertility is currently considered to be a major problem in Iran. According to published articles, one in four Iranian couples is infertile (1). Infertility treatment results in numerous economic losses and mental problems. Polycystic ovary syndrome (PCOS) is the most common cause of infertility (1). In Iran, the prevalence of PCOS is 6%. PCOS is caused by excessive production of luteinizing hormone (LH), which results in the formation of ovarian cysts, hyperandrogenism, hyperinsulinemia, insulin resistance, acne, hirsutism, and obesity (2). Previous studies have shown that women with body weight above or below normal are at high risk of infertility (3). One of the symptoms of PCOS is obesity; thus, in such patients, the expansion of fatty tissue may be the result of greater leptin production. Leptin has a critical role in the control of ovulation (3, 4). Patients with PCOS may experience leptin resistance that ultimately results in infertility (4). Therefore, the aim of this study was to investigate serum and follicular fluid leptin concentrations in infertile women with PCOS.

The study was conducted in accordance with ethical procedures and policies approved by the Ethical Committee of Ahvaz Jondishapour University of Medical Sciences, Ahvaz, Iran and Helsinki Declaration of 1975. Informed consent was obtained from all patients and controls. A case-control study was conducted. The case group consisted of 30 infertile women with PCOS, who were admitted to the Infertility Department of Imam Khomayni Hospital in Ahvaz, Iran. Patients had previously been diagnosed with PCOS and infertility by a specialist via ultrasound and clinical and biochemical findings. The case group was undergoing oocyte retrieval in stimulated cycles for *in vitro* fertilization (IVF). Our control group consisted of 30 healthy fertile women adjusted for age and body mass index (BMI) with the case group. Subjects with infections, diabetes mellitus, renal failure, and hypertension, anorexia, or digestive tract abnormalities were excluded from the study. Age, body weight, and height were measured and BMI was calculated. On day 14 of their menstrual cycle 5 ml blood was collected from all subjects in both groups. Blood was centrifuged at 2000 rpm for 10 min. Serum was separated and stored at  $-80^{\circ}\text{C}$  until measurement. Using an ultrasound-guided transvaginal needle, human luteinized granulosa cells were collected from the ovaries of subjects in the case group. Follicular fluid was frozen immediately in liquid nitrogen and stored at  $-80^{\circ}\text{C}$ . Serum and follicular fluid leptin concentrations were determined by the enzyme linked immunosorbent assay (ELISA). The Biovendor kit was used for measurement of leptin concentrations. The normal range of serum leptin was considered 12-23 (ng/ml) (5).

All data were analyzed using statistical package for the social sciences (SPSS) software (version 17.0, Nie, Bent & Hull, USA). and t-test. The mean age was  $33.6\pm 2.5$  years in the control group and  $30.9\pm 3.7$  years in the case group. Serum leptin concentrations were not associated with age in either group ( $p=0.904$  in control group and  $p=0.216$  in case group). There was not a noticeable difference between mean BMI in the control and case groups (27.4 vs. 27.2  $\text{kg}/\text{m}^2$ ). There was a positive relationship between serum leptin concentrations and BMI in the control ( $p=0.005$ ,  $r=0.516$ ) and case groups ( $p=0.006$ ,  $r=0.547$ ). In the case group, the association between follicular fluid leptin concentrations and BMI was not significant ( $p=0.141$ ). In the case group, serum leptin concentrations were consistent with follicular fluid ( $p<0.001$ ,  $r=0.839$ ). Comparison of serum leptin concentrations between cases and controls revealed no significant

difference ( $p=0.56$ ). This study aimed to investigate changes in serum and follicular fluid leptin concentrations among infertile women with PCOS and healthy fertile women. Our study showed no significant relationship between age and leptin concentrations. However, Zhong *et al* revealed that serum leptin concentrations varied with age. This may be explained by the fact that our study groups were at a pre-menopausal stage, whereas the study group in Zhong *et al* work consisted of both pre- and post-menopausal women, and the mean age of the study group ( $45.4 \pm 14.8$  years) was higher than that of our study groups ( $33.6 \pm 2.5$  and  $30.9 \pm 3.7$  years). We found a positive correlation between serum leptin concentrations and BMI, which is similar to the findings of Zhong *et al* (6).

In our investigation, a noticeable correlation was observed between serum leptin concentrations and BMI. This is in accordance with the findings of Pehlivanov *et al* (7). Leptin originates from fatty tissue; thus, an increase in body fat results in more leptin production (8). Therefore, our results are reasonable. However, a correlation was not observed between follicular fluid leptin concentrations and BMI in the case group. In contrast, Fedorcsak *et al* reported a positive correlation between these two variables (9). We found positive correlations between serum and follicular fluid concentrations in the case group. Studies by Fedorcsak *et al* confirm our findings (9). In our study, there was no significant difference between leptin concentrations among the cases and controls; this result is in agreement with the findings of Lu *et al* (10). Based on our study results, no noticeable changes in serum or follicular fluid leptin concentrations were observed in patients with PCOS. Therefore, infertility in patients with PCOS is not a consequence of changes in leptin concentrations. Studies on the effects of other metabolic factors on infertility in such patients are recommended.

### Acknowledgements

Authors thank Personnels of Infertility Department of Imam Khomayni Hospital in Ahvaz, Iran for collecting the samples. This work was supported by Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

**Dian Dayer<sup>1</sup> M.Sc., Roshan Nikbakht<sup>2</sup> M.D., Manijeh Kadkhodai Elyaderani<sup>3</sup> Ph.D.**

1. Department of Laboratory Sciences, Para Medical Faculty, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

2. Department of Obstetrics and Gynecology, Fertility and Perinatology Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

3. Department of Biochemistry, Medicine Faculty, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

### Corresponding Author:

Dian Dayer, Department of Laboratory Sciences, Para Medical Faculty, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

Email: dayer86@gmail.com

Tel/Fax: (+98) 9163149254

Received: 15 September 2012

Revised: 13 December 2012

Accepted: 31 August 2013

### References

- Vahidi S, Ardalan A, mohammad K. Prevalence of Primary Infertility in the Islamic Republic of Iran in 2004-2005. *Asia Pac J Public Health* 2009; 21: 287-293.
- Tehrani FR, Simbar M, Tohidi M, Hosseinpanah F, Azizi F. The prevalence of polycystic ovary syndrome in a community sample of Iranian population: Iranian PCOS prevalence study. *Reprod Biol Endocrinol* 2011; 9: 39.
- Moschos S, Chan JL. Leptin and reproduction: a review. *Fertil Steril* 2002; 77: 433-444.
- Sabogal JC, Munoz L. Leptin in obstetrics and gynecology: a review. *Obstet Gynecol Surv* 2001; 56: 225-230.
- Chow TK, Phoon MC. Measurement of serum leptin concentrations in university undergraduates by competitive elisa reveals correlations with body mass index and sex. *Adv Physiol Educ* 2003; 27: 70-77.
- Zhong N, Wu XP, Xu ZR, Wang AH, Luo XH, Cao XZ, et al. Relationship of serum leptin with age, body weight, body mass index, and bone mineral density in healthy mainland Chinese women. *Clin Chim Acta* 2005; 351: 161-168.
- Pehlivanov B, Mitko M. Serum leptin levels correlate with clinical and biochemical indices of insulin resistance in women with polycystic ovary syndrome. *Eur J Contraceptreprod Health Care* 2009; 14: 153-159.
- Mantzoros CS. Role of leptin in reproduction. *Ann NY Acad Sci* 2000; 900: 174-183.
- Fedorcsak P, Storeng R, Dale PO, Tanbo T, Torjesen P, Urbancsek J, et al. Leptin and leptin binding activity in the preovulatory follicle of polycystic ovary syndrome patients. *Scand J Clin Lab Invest* 2000; 60: 649-655.
- Lu XP, Wang B, Huang HF. [Expression of leptin mRNA in luteinized granulosa cells and leptin levels in serum and follicular fluid of non-obese infertile patients with polycystic ovary syndrome]. *Zhonghua Yi Xue Za Zhi* 2005; 85: 88-91. (In Chinese)