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Original Article

Overweight and obesity adversely affect outcomes of assisted reproductive technologies in polycystic ovary syndrome patients

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Abstract: Overweight and obesity may have negative impact on IVF/ICSI treatment outcomes. However, it is not clear whether overweight and obesity have impact on IVF/ICSI outcomes in PCOS patients. The aim of this study was to examine the effect of overweight and obesity on IVF/ICSI treatment outcomes in PCOS patients treated with GnRH agonist long protocol. This retrospective study was conducted in a reproductive medicine center from January 2009 to June 2013. IVF/ICSI characteristics and outcomes were analyzed in 688 PCOS patients according to their BMI. A total of 409 normal weight patients (group A, 18.5 kg/m^2 ≤ BMI <24 kg/m^2) and 279 overweight and obese patients (group B, BMI ≥24 kg/m^2) were included into this study. Patient age, basal FSH, basal LH and peak E2 concentration were comparable in the two groups. Compared with patients in group A, patients in group B had similar number of retrieved oocytes, 2PN, and high quality embryos. However, overweight and obese women needed more ampoules of gonadotrophin and longer days of stimulation. In addition, the implantation rate (38.3% vs. 35.6%; P=0.000) was also higher in normal weight patients. Overweight and obese women seemed to have lower clinical pregnancy rate (56.9% vs. 53.4%; P>0.05), but the difference was not statistically significant. In conclusion, overweight and obesity is associated with unfavorable IVF/ICSI outcomes in PCOS patients treated with GnRH agonist long protocol.

Keywords: Overweight, obese, PCOS, in vitro fertilization

Introduction

Overweight and obesity, one of the greatest nutritional problems in the world, are evidenced to have relationship with an increased risk of infertility [1-3]. According to several published literatures, the prevalence of overweight in Chinese women was 13.1% in 1991 [4], and increased to 21.7% 10 years later [5]. Body mass index (BMI), calculated as weight in kilograms divided by height in meters, is considered to be the common measure of overweight and obesity. Up to date, many studies of the impact of BMI on outcomes of in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI) treatment have been conducted, while the results are conflicting. Some investigators showed no significant impact of BMI on response to ovarian stimulation, and pregnancy outcomes [6-8]. In contrast, other studies have demonstrated that overweight and obesity may adversely affect cumulative live birth rates [9], increase risk of spontaneous abortion [10, 11].

Polycystic ovary syndrome (PCOS) is a heterogeneous and endocrine disorder that affects 6-10% of women of reproductive age [12, 13]. It is not rare to see PCOS patients attending reproductive medicine center, because PCOS account for nearly 73% of anovulatory infertility cases [14], and 40%-60% of women with PCOS are overweight or obese [15]. However, the impact of overweight and obesity on assisted reproductive technologies outcomes in patients with PCOS is still unknown, because data analyzing IVF/ICSI outcomes in PCOS patients are limited. Thus, the aim of this study is to assess whether overweight or obese PCOS patients treated with GnRH agonist long protocol have the same outcomes of IVF/ICSI when compared with normal weight patients.

Table 1. Characteristics of IVF/ICSI treatment according to BMI

	Group A 18.5 kg/m^2 ≤ BMI <24 kg/m^2	Group B BMI ≥24 kg/m^2	*P* value
No. of patients	409	279	
Age (years)	28.3±4.0	29.1±4.1	NS
Basal FSH (mIU/mL)	6.6±1.8	6.1±1.4	NS
Basal LH (mIU/mL)	9.2±10.5	8.7±6.2	NS
BMI (kg/m^2)	21.5±1.4	26.8±2.3	0.000
Days of stimulation	11.9±1.7	12.4±2.1	0.000
Total Gonadotropins (IU)	1491.5±503.1	1765.3±623.4	0.000
Peak E2 (pg/mL)	7842.4±4869.8	6379.4±3139.0	0.000
No. of oocytes retrieved	16.1±7.3	16.1±8.3	NS
No. of fertilized oocytes (2PN)	11.1±5.7	10.7±6.0	NS
No. of high quality embryos	7.9±4.6	7.5±4.7	NS

Note: Data are presented as mean ± SD unless otherwise indicated. NS: non-significant (*P* value is >0.05).

Table 2. IVF/ICSI treatment outcomes according to BMI

	Group A 18.5 kg/m^2 ≤ BMI <24 kg/m^2	Group B BMI ≥24 kg/m^2	*P* value
No. of patients	409	279	
No. of embryo transferred	1.9±0.5	1.8±0.5	NS
Implantation rate (%)	189/493 (38.3)	109/306 (35.6)	0.000
Clinical pregnancy rate (%)	152/267 (56.9)	93/174 (53.4)	NS

NS: non-significant (*P* value is >0.05).

Materials and methods

Subjects and study design

A total of 688 women with PCOS who underwent their first IVF or ICSI treatment from January 2009 to June 2013 in our center were included in this retrospective cohort study. All these patients diagnosed with PCOS met the Rotterdam 2003 criteria and underwent IVF/ICSI treatment using GnRH agonist long protocol [16]. According to their BMI, the patients were divided into two groups: Group A included 409 patients with BMI ≥18.5 kg/m^2 and <24 kg/m^2; group B included 279 overweight and obesity patients with BMI ≥24 kg/m^2.

Patients treated with standard mid-luteal phase GnRH agonist long protocol commenced pituitary suppression with leuprolide acetate (Diphereline 0.1 mg, Beaufour, Ipsen, Pairs, France) at a dose of 0.1 daily. Once pituitary suppression was achieved with a serum E2 <30 mIU/mL and LH <3 mIU/mL, recombinant FSH (Gonal-F, Serono, Switzerland) were given at a dose of 150-450 IU alone or in combination with hMG (hMG, Lizhu, China).

Transvaginal ultrasounds were performed to monitor follicular response, upon which we adjusted the dose of gonadotropins. When two or more follicles had reached a diameter of 17 mm, urinary hCG 10 000 IU was administered to trigger ovulation. 34-36 hours after that, oocyte retrieval was performed under the guidance of ultrasounds. Routine IVF or ICSI procedures were followed, and 2 embryos were transferred 3 days after oocyte retrieval. However, if patients were diagnosed with severe OHSS and hospitalized, embryos would be cryopreserved and thawed to transfer at least 2 month later. For luteal phase progesterone supplement, 60 mg of progesterone in oil was given everyday.

Fertilization rate was defined as percentage of fertilized embryos (2PN) in all the mature oocytes. Implantation rate was calculated as the fraction of embryos transferred resulting in gestational sac(s). Pregnancies mentioned in this study were clinical pregnancies where one or more gestational sacs and heart beat were confirmed by transvaginal ultrasound 4 weeks after embryos transfer.

Statistics

Data were expressed as mean ± SD and analyzed using SPSS version 15.0 (SPSS Inc., Chicago, IL, USA). Means were analyzed using

the two-tailed t-test for parametric data, and proportions were compared using the Chi-square test. In all cases, statistical significance was set at $P<0.05$.

Results

A total of 688 PCOS women who had their first stimulation cycle using GnRH agonist long protocol were included in the statistical analysis. The comparison of characteristics of IVF/ICSI treatment between group A and group B was presented in **Table 1**. There were no significant differences between groups regarding mean age, basal FSH and basal LH. Patients with a BMI ≥24 kg/m^2 needed more ampoules of gonadotrophin and longer days of stimulation. Overweight and obese patients also had significantly lower peak E2 level on HCG administration day. However, compared with the normal weight patients, the overweight and obese ones had comparable number of oocytes retrieved, fertilized oocytes and high quality embryos.

The IVF/ICSI treatment outcomes were described in **Table 2**. The number of transferred embryos and fertilization rate were comparable in the two groups. However, compared with patients in group B, normal weight patients in group A had higher implantation rate (38.3% vs. 35.6%; P=0.000). Overweight and obese women seemed to have lower clinical pregnancy rate (56.9% vs. 53.4%; P>0.05), but the difference was not statistically significant.

Discussion

Multiple studies have reported the impact of overweight and obesity on the outcomes of assisted reproductive technologies, but the conclusions are controversial. In addition, it is rare to see data based on PCOS patients undergoing IVF/ICSI treatment. To the best of our knowledge, this study was the largest dataset about the impact of overweight and obesity on IVF/ICSI treatment in PCOS patients using GnRH agonist long protocol.

It was found that PCOS patients with increased BMI required more gonadotropin and longer days of stimulation to achieve follicular maturation, but the peak E2 level was significantly lower in overweight and obese patients. Patients in two groups had similar number of retrieved oocytes, but overweight and obese ones had lower number of fertilized oocytes and high quality embryos, even the difference was not statistically significant. The reason for this may be because the quality of retrieved oocytes in overweight and obese people is worse than that of normal weight people. Our results are similar with the study of McCormick, who also found lean PCOS patients tended to have favorable IVF characteristics when compared with obese group, even though the clinical outcomes were not different [17]. Another systematic review also showed that patients with increased BMI required higher dose of gonadotrophin [18]. These differences may be explained by the reduced ovarian response [19, 20] and suppressed oocyte developmental competence [21].

Although no statistical difference in fertilized oocytes was observed in the two groups, normal weight patients had significantly higher implantation rate and seemed to have higher clinical pregnancy rate. These observations also could be seen from another comparison of 19 morbid obese PCOS patients with BMI ≥40 kg/m^2 with 53 non-morbidly obese PCOS patients, indicating that morbid obesity was associated with significantly lower pregnancy rate, and also slightly lower live birth rate [22]. Recently, a large retrospective study with 6500 cycles showed that pregnancy rate and live birth rate were reduced progressively with increasing BMI, without affecting the embryo quality [23]. In addition, Onalan et al reported that obesity was not only positively correlated with the occurrence of polyps, but also an independent prognostic factor for the development of endometrial polyps according to logistic regression analysis [24]. All these results indicate that may be it is the alteration of uterine environment that impairs IVF/ICSI outcome in overweight and obese patients.

This study is limited by its retrospective design, and number of pregnant case in the overweight and obese group is small. Furthermore, many patients still have several embryos cryopreserved in our center and the cumulative live birth rate and live birth rate could not be assessed.

In conclusion, this study demonstrated that overweight and obese PCOS patients undergoing IVF/ICSI treated with GnRH agonist long pro-

tocol had unfavorable outcomes compared with normal weight patients. For PCOS patients with elevated BMI, it appears that weight loss programme is recommendable prior to IVF/ICSI treatment.

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Disclosure of conflict of interest

None.

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