

Original Article

Effect of overweight/obesity on IVF-ET outcomes in chinese patients with polycystic ovary syndrome

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Received November 5, 2014; Accepted November 8, 2014; Epub December 15, 2014; Published December 30, 2014

Abstract: The purpose of this study was to investigate the impact of body mass index (BMI) on the outcomes of IVF/ICSI treatment cycles in Chinese patients with polycystic ovary syndrome (PCOS). Women with PCOS (n = 128) and tubal factor (n = 128) underwent a conventional long GnRH agonist suppressive protocol. Women with PCOS had significantly more oocytes retrieved (P < 0.05) and available embryos (P < 0.05), as compared to patients with tubal infertility. No significant differences were observed in clinical pregnancy rate, miscarriage rate and live birth rate between two groups. Patients were further divided into two subgroups. In total, 49 patients in PCOS group and 19 patients in tubal factor group were overweight or obese (BMI ≥ 24 kg/m²). Lean women (BMI < 24 kg/m²) with PCOS showed higher clinical pregnancy rate (P < 0.05). Live birth rate and miscarriage rate were also higher in lean PCOS women, but the differences were not significant. Similar clinical outcomes of IVF/ICSI success were achieved between two subgroups in tubal factor patients. In conclusion, lean PCOS patients obtained higher clinical pregnancy rate compared with overweight/obese PCOS patients in Chinese populations.

Keywords: Overweight/obesity, PCOS, IVF/ICSI outcome, pregnancy, live birth

Introduction

Polycystic ovary syndrome (PCOS) is an endocrine disorder that affects approximately 5-10% women of reproductive age [1, 2] and has been linked to multiple metabolic changes, such as obesity, insulin resistance and type 2 diabetes [3-5]. Patients can be diagnosed with PCOS if they meet any two of three criteria after exclusion of other causes: oligoovulation and/or anovulation, clinical or biochemical hyperandrogenism, and polycystic ovaries by ultrasound [6].

PCOS is the most common cause of anovulatory infertility, accounting for an important proportion of women seeking fertility treatment [7]. PCOS is regularly associated with overweight and obesity. Regardless of PCOS, obese women may achieve less favorable ART outcomes [8, 9]. In a systematic review on the effect of body mass index and IVF-ET outcomes, Vivian concluded that women with BMI ≥ 25 kg/m² showed lower clinical pregnancy and live

birth rates, but higher miscarriage rates when undergoing IVF/ICSI treatment [10]. According to the same review, more studies considering the impact of causes of infertility should be conducted, particularly polycystic ovary syndrome.

Data referring to the relationship between obesity, PCOS and IVF/ICSI outcomes are inconsistent. Compared to non-obese PCOS patients, obese women with PCOS may have less retrieved oocytes, increased miscarriage rates and lower clinical pregnancy rates [11-13]. In contrast, some reports proposed that obese and non-obese PCOS patients show no significant differences on IVF/ICSI outcomes [1, 14]. The reasons may be due to different cut-off points for BMI, discrepancy of inclusion criteria among studies, and/or varying focus of outcomes measures.

A report from World Health Organization revealed that Asian populations may have different cut-off points for BMI than do European populations [15]. Meanwhile, epidemiology

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Table 1. Comparison between IVF/ICSI cycles in the patients with PCOS and tubal factor

Variable	PCOS	Tubal factor	P-value
Number of cycles	128	128	-
Patient age (years)	29.8 ± 3.7	30.0 ± 3.3	NS
Bodyweight (kg)	59.3 ± 9.7	53.9 ± 6.6	0.000
BMI (kg/m ²)	23.1 ± 3.6	21.2 ± 2.5	0.000
Number of oocytes retrieved	14.3 ± 6.1	12.2 ± 5.6	0.003
Number of available embryos	8.9 ± 4.5	7.3 ± 3.8	0.002
Clinical pregnancy rate (%)	49/128 (38.3)	39/128 (30.5)	NS
Miscarriage rate (%)	6/50 (12.0)	3/39 (7.7)	NS
Live birth rate (%)	44/128 (34.4)	36/128 (28.1)	NS

Values are mean ± SD and n/total (%). NS = not statistically significant.

studies from China recommended that Chinese adults with a BMI of ≥ 24 kg/m² and ≥ 28 kg/m² would be defined as overweight and obesity, respectively [16, 17]. Data concerning the impact of overweight and obesity on IVF treatment in Chinese women were inconsistent [18, 19]. The present study was performed to assess whether BMI affects IVF/ICSI outcomes in Chinese women with PCOS.

Materials and methods

This was a retrospective cohort study of patients undergoing IVF/ICSI treatment in reproductive medicine center of Tongji Hospital between January 2009 and June 2011. A total of 128 patients with PCOS were enrolled. According to age (± 1 year) and initiation of IVF/ICSI cycle, a non-random 1:1 matched sample was selected from infertile women with tubal factor disease who had received IVF/ICSI treatment within the same period at the reproductive medicine center. Only the first cycle of each patient was included. Exclusion criteria were: oocyte or sperm donation, in vitro maturation, preimplantation genetic diagnosis, testicular sperm aspiration, frozen embryo transfer, blastocyst transfer, patients with endometriosis or metabolic diseases which may lead to abnormal BMI such as diabetes, and cycles not resulting in fresh embryo transfer. Based on the recommended Chinese BMI cut-off points, study subjects were divided into two subgroups (BMI < 24 kg/m² and BMI ≥ 24 kg/m²). Institutional Review Board approval was not necessary because this is a retrospective analysis of conventionally treated patients, no intervention was involved except routine and standard IVF preparation and treatment, the data were

anonymous, and no patient-identifying information was included.

Women with PCOS were chosen using the Rotterdam criteria [6]. Tubal factor infertility was diagnosed by hysterosalpingography combined with laparoscopy. All patients in this study underwent controlled ovarian hyperstimulation with long luteal phase GnRH agonist protocol as previously described [20]. The main outcome measures were clinical pregnancy and live birth. Clinical

pregnancy was defined as observation of the intrauterine gestation sac and fetal cardiac activity by transvaginal ultrasound at 6-7 weeks of gestation. Live birth was defined as any deliveries in which at least one baby was born alive and survived for more than 1 month.

Statistical analysis was performed using SPSS version 13.0 (SPSS, Chicago, IL, USA). Differences between continuous variables were analysed with Student's t test and categorical variables were compared using Chi-square test. Results are presented as mean \pm SD. P values less than 0.05 were considered to be significant.

Results

A total of 128 patients with PCOS and 128 patients with tubal factor were involved in this study. There was no significant difference observed between two groups in regards to age (29.8 \pm 3.7 versus 30.0 \pm 3.3). Bodyweight and BMI were significantly higher (both $P < 0.01$) in patients with PCOS compared to women with tubal factor. Number of oocytes retrieved and available embryos differs significantly between two groups (14.3 \pm 6.1 versus 12.2 \pm 5.6, $P = 0.003$ and 8.9 \pm 4.5 versus 7.3 \pm 3.8, $P = 0.002$, respectively). No significant differences were observed between patients with PCOS and tubal factor regarding clinical pregnancy rate, miscarriage rate and live birth rate (Table 1).

In the PCOS group, 49 out of 128 patients were overweight and obese (BMI ≥ 24 kg/m²), compared with 19 out of 128 patients in the tubal factor group. Lean patients (BMI < 24 kg/m²)

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Table 2. Characteristics of all IVF/ICSI treatments in patients with PCOS and tubal factor according to body mass index (BMI)

Variable	PCOS		P-value	tubal factor		P-value
	BMI < 24 kg/m ²	BMI ≥ 24 kg/m ²		BMI < 24 kg/m ²	BMI ≥ 24 kg/m ²	
Number of cycles	79	49	-	109	19	-
Patient age (years)	29.4 ± 3.4	30.5 ± 4.1	NS	29.7 ± 3.1	31.5 ± 4.2	0.034
Number of oocytes retrieved	14.9 ± 6.2	13.4 ± 5.9	NS	12.1 ± 5.6	12.4 ± 5.4	NS
Number of available embryos	9.0 ± 4.3	8.8 ± 4.8	NS	7.3 ± 3.9	7.6 ± 3.0	NS
Clinical pregnancy rate (%)	37/79 (46.8)	13/49 (26.5)	0.022	33/109 (30.3)	6/19 (31.6)	NS
Miscarriage rate (%)	5/37 (13.5)	1/13 (7.7)	NS	3/33 (9.1)	0/6 (0.0)	NS
Live birth rate (%)	32/79 (40.5)	12/49 (24.5)	NS	30/109 (27.5)	6/19 (31.6)	NS

Values are mean ± SD and n/total (%). NS = not statistically significant.

with PCOS showed more oocytes retrieved than overweight and obese PCOS women (14.9 ± 6.2 versus 13.4 ± 5.9, $P = 0.165$), but no significant difference was observed. Regarding age and total number of embryos, there were no significant differences between two subgroups (BMI < 24 kg/m²; BMI ≥ 24 kg/m²). Lean patients had a significantly higher clinical pregnancy rate (46.8% versus 26.5%, $P = 0.022$) compared to overweight and obese patients in PCOS group. Comparisons of lean versus overweight and obese women showed live birth rates of 40.5% versus 24.5% ($P > 0.05$) and miscarriage rates of 13.5% versus 7.7% ($P > 0.05$), respectively (**Table 2**).

For patients with tubal factor, lean women was significantly younger than overweight and obese women (29.7 ± 3.1 versus 31.5 ± 4.2, $P = 0.034$). No differences were seen between two subgroups concerning the rest of clinical characteristics (**Table 2**).

Discussion

The present study was designed to investigate the effects of overweight and obesity on IVF/ICSI success in women with PCOS. Compared to patients with tubal factor, PCOS women had higher body weight and BMI. As expected, PCOS led to more retrieved oocytes and available embryos. The reason could be associated with pathogenesis of the syndrome. PCOS is an endocrine disease which may result in obesity and hyperstimulation status [5, 21]. Irrespective of BMI, PCOS women in our study achieved similar clinical outcomes as tubal factor women when undergoing the midluteal long GnRH agonist protocol. These findings are in relation to previous reports [22].

This study found that PCOS women with a BMI of ≥ 24 kg/m² had lower clinical pregnancy

rates than overweight/obese women. The result is in accordance with a study conducted by Orvieto and his co-workers. Moreover, an apparently (but not significantly) higher live birth rate was found in lean PCOS patients, and this result suggests that a larger study sample would disclose the negative relationship between overweight/obesity and live birth rate. For women with tubal infertility, lean patients were younger than overweight/obese patients. Due to the small sample size, our study was limited to show differences in the clinical pregnancy rates and live birth rates between two subgroups in tubal factor patients, which are contrary to other studies.

Existing studies linking obesity and PCOS to outcomes of IVF/ICSI treatment were limited and controversial. In a recent study, outcomes of IVF/ICSI were compared between lean and obese women with or without PCOS [14]. There was a trend of increased clinical pregnancy rate, increased live birth rate and decreased miscarriage rate, although no statistically significant were observed. Similarly, study managed by Beydoun and his colleagues revealed that categorical BMI (< 25, 25-29.9, ≥ 30) did not affect outcome measures of infertility treatment success [1]. However, Orvieto found that PCOS patients with BMI ≤ 25 kg/m² showed significantly higher clinical pregnancy rate compared to those with BMI > 25 kg/m² undergoing a standard long GnRH agonist protocol [12]. In another study, obese PCOS women experienced higher miscarriage rates than non-obese PCOS women in ICSI cycles [13].

Obesity can inversely affect oocyte size, oocyte and embryo quality in PCOS women [23, 24]. This may be associated with the alteration of follicle androgen profiles, insulin resistance

and elevated leptin levels. The British Fertility Society has recently recommended that women undergoing infertility treatment should defer treatment until a BMI of < 35 kg/m² is achieved [25]. As obesity is an increasing problem among women of reproductive age, such guidelines would be helpful, especially for women with PCOS. More studies concerning obesity and PCOS in Chinese women seeking infertility treatment should be performed. Prospective studies comparing ART outcomes before and after weight loss approaches are also beneficial.

In summary, our results indicated that although patients with PCOS have more retrieved oocytes and available embryos, similar clinical outcomes are achieved comparing to women with tubal infertility. Meanwhile, lean PCOS women achieved significantly higher clinical pregnancy rate and apparently higher live birth rate. Overweight and obese PCOS patients should be encouraged to lose weight before initiation of ART.

Acknowledgements

This study was supported by grants from the National Natural Science Foundation of China (No. 81170619).

Disclosure of conflict of interest

None.

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