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ASSISTED REPRODUCTION TECHNOLOGIES

Effect of body mass index on the outcomes of controlled ovarian hyperstimulation in Chinese women with polycystic ovary syndrome: a multicenter, prospective, observational study

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Abstract
Purpose The purpose of the present study is to explore the influence of body mass index (BMI) on outcomes of in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI) techniques in Chinese women with polycystic ovary syndrome (PCOS).
Methods This was a multicenter, prospective, observational study that enrolled 800 subjects with PCOS from nine hospitals in China. Patients were categorized according to BMI categories: underweight, <18.5 kg/m^2; normal, 19–23.9 kg/m^2; overweight, 24–27.9 kg/m^2; and obese, ≥28 kg/m^2. Total recombinant follicle-stimulating hormone (rFSH) dose used, estradiol, and progesterone levels on human chorionic gonadotropin (hCG) day; implantation rate; and biochemical, clinical, and ongoing pregnancy rates were compared among BMI categories. Hormone levels (estradiol, follicle-stimulating hormone (FSH), LH, testosterone, and progesterone) were measured using electrochemiluminescence assays.
Results Among the 774 subjects, 27.3 % were overweight and 8.1 % were obese. The rFSH dose used differed significantly among BMI categories ($P < 0.001$). The implantation rate was lower in obese subjects than that in normal-weight subjects (25.3 vs 45.7 %). Clinical pregnancy rate per transfer differed among BMI categories ($P = 0.033$), but there was no difference for biochemical ($P = 0.327$) and ongoing ($P = 0.084$) pregnancy rates. The miscarriage rate was similar among BMI categories.
Conclusions More than one third of Chinese women with PCOS undergoing IVF/ICSI are overweight or obese. Elevated BMI is associated with reduced clinical pregnancy rate but similar ongoing pregnancy rates, suggesting that BMI has little impact on IVF outcomes.

Keywords Polycystic ovary syndrome · In vitro fertilization · Intracytoplasmic sperm injections · Body mass index · Pregnancy rate

Capsule Elevated body mass index is associated with reduced clinical pregnancy rate but similar ongoing pregnancy rates.

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Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women of childbearing potential, affecting 6–7 % of women at a reproductive age. Indeed, PCOS accounts for nearly 73 % of the cases of anovulatory infertility

[1]. Assisted reproductive technology (ART) has become an important option for patients with PCOS who wish to become pregnant. The application of in vitro fertilization (IVF) techniques in women with PCOS has grown over the years, due to progressive improvements in IVF outcomes, the use of single embryo transfer, and a decrease in multiple pregnancy rates. IVF treatment is indicated in patients with PCOS who (a) ovulate but have had a failed pregnancy after ovarian stimulation; (b) do not ovulate in response to repeated ovarian stimulation or assisted treatment; or (c) have concomitant infertility factors, such as tubal or male factor. However, there is a high risk of ovarian hyperstimulation syndrome (OHSS) in patients with PCOS undergoing IVF treatment. In addition, poor zygote quality, a lower fertilization rate than women without PCOS, and a high rate of cycle cancellations remain common problems contributing to IVF cycle failure in patients with PCOS [2].

Choosing an optimal controlled ovarian hyperstimulation (COH) protocol is the key to the success and safety of ART. The protocol for COH should take into consideration drug combinations, initial dose, dosage adjustment, and the timing of human chorionic gonadotropin (hCG) injection, as well as the number of high-quality follicles and the incidence of OHSS. Gonadotropin-releasing hormone agonist (GnRH-a) long protocol is one of the common regimens for ovarian stimulation in women with PCOS [3]. Human recombinant follicle-stimulating hormone (rFSH) alpha has been widely used for COH, as it induces a stable ovarian response, its administration can be individually tailored, and less frequent monitoring is required [4]. Thus, the use of rFSH can potentially reduce the risks of cycle cancellation and OHSS in patients with PCOS.

The success of ART in women with infertility is affected by a number of factors, including age, obesity, and ovarian reserve. Previous studies have reported that body mass index (BMI) can influence the success rate of IVF and embryo transfer treatments in patients with PCOS [5]. International studies outside China have shown that 35–65 % of patients with PCOS are obese [2]. The distribution of BMI differs among Asians and populations in Europe and the USA. Asians generally have a higher percentage of body fat than White people of the same age, sex, and BMI; thus, Asians are believed to have higher health risks [6]. Furthermore, the prevalence of overweight and obesity has been increasing in China. In 1991, 13.1 % of females were overweight in China, whereas in 2001, this had increased to 21.7 %, with 3.73 % of females considered obese [7]. In view of this, it is possible that a significant proportion of women with PCOS have a BMI outside the normal range and that this may represent an important factor influencing the outcomes of IVF in these women.

A small number of studies have examined some of the relationships between PCOS, BMI, and the outcomes of IVF/intracytoplasmic sperm injection (ICSI). A recently published retrospective study found that in Chinese women undergoing IVF, being overweight affected the ovarian response and was associated with an increased rate of miscarriage; however, this study did not include women with PCOS. Another investigation reported that the use of exogenous follicle-stimulating hormone (FSH) for PCOS, BMI, the patient's history (anovulation or irregular menstruation), baseline FSH level, and the number of antral follicles were factors that predicted the ovarian response [8]. To date, there have been no large-scale studies of the factors influencing IVF outcomes in Chinese women with PCOS. Therefore, we designed and carried out this observational, prospective, and multicenter study, in order to evaluate the effects of BMI on the outcomes of a long downregulation protocol with recombinant FSH (rFSH) for COH.

Materials and methods

Study subjects

Between August 2011 and April 2013, women with PCOS undergoing IVF/ICSI, using rFSH and a long downregulation protocol, at nine hospitals in China (Supplementary Table S1) were enrolled in the study. The inclusion criteria were as follows: (1) women with infertility aged 20–35 years; (2) PCOS had been diagnosed according to the criteria published by the Chinese Ministry of Health in July 2011 which is consistent to the Rotterdam criteria in 2003 (Supplementary Table S2); (3) indications for IVF/ICSI treatment had been met (IVF: women who had repeatedly failed to become pregnant with ovulation-induction treatment or had concomitant infertility factors; ICSI: severe oligozoospermia or non-ejaculated sperms or failed egg fertilization with conventional IVF); (4) rFSH was used for COH; and (5) downregulation was achieved with a long protocol based on triptorelin and Diphereline. The subject was excluded from the study if any of the following exclusion criteria were applied: (1) baseline FSH >12 IU/L; (2) previous IVF/ICSI treatment on three or more occasions; (3) previous experience of moderate-to-severe OHSS; (4) a history of diabetes mellitus, hyperthyroidism, or hypothyroidism; (5) hyperandrogenemia caused by other factors; (6) violations of the product insert; (7) use of urinary human menopausal gonadotropin/FSH in the current treatment cycle; or (8) hypersensitivity to rFSH or its excipients. All study subjects were fully informed of the nature of the study and provided written consent for inclusion. The study was approved by the ethics committees of the participating hospitals (Supplementary Table S1).

Study design

This was a multicenter, prospective, observational study conducted in China that was designed to enroll a total of

800 subjects with PCOS. The dosage of rFSH for COH was adjusted according to the requirements of each individual subject. The treatment regimen used was based on the routine COH protocol at each site. The monitoring of the study procedures and collection of data were carried out during seven separate visits (Supplementary Table S3): visit 1 (collection of baseline data and demographic characteristics), visit 2 (downregulation and ovarian stimulation with rFSH), visit 3 (administration of hCG and measurement of follicle size), visit 4 (embryo transfer), visit 5 (test for biochemical pregnancy using measurement of urinary or blood hCG), visit 6 (evaluation of clinical pregnancy using ultrasound), and visit 7 (evaluation of ongoing pregnancy until 12 weeks after embryo transfer and assessment of the occurrence and severity of OHSS).

Subjects who completed all assessments up to and including the last visit (visit 7) were deemed to have completed the study.

Outcome measures

The outcome measures included comparisons of the following variables among the various BMI categories: total dose of rFSH used, number of oocytes retrieved, number of embryos, number of embryos transferred, implantation rate (defined as the number of gestational sacs detected by ultrasound 4–5 weeks after transfer/the number of embryos transferred × 100 %), biochemical pregnancy rate per stimulation cycle and per transferred cycle, clinical pregnancy rate per stimulation cycle and per transferred cycle, ongoing pregnancy rate per stimulation cycle and per transferred cycle, and miscarriage rate during the first trimester (defined as the number of subjects with miscarriage during the first 12 weeks/the number of subjects with clinical pregnancy × 100 %).

BMI was measured as the mass in kilograms divided by the square of the height in meters. The subjects were classified into the following categories according to their BMI: underweight (<18.5 kg/m^2), normal (19–23.9 kg/m^2), overweight (24–27.9 kg/m^2), and obese (≥28 kg/m^2), based on the 2002 recommendations of the Bureau of Disease Control, Chinese Ministry of Health [9–11].

Hormone level measurement

Blood was sampled at each visit. Hormone levels (estradiol, FSH, LH, testosterone, and progesterone) were measured using electrochemiluminescence assays on the Elecsys platform (Roche Diagnostics, Basel, Switzerland) using the reagents supplied by the manufacturer.

Safety analysis

All adverse events (AEs) that occurred during the study were recorded using the medical dictionary for drug regulatory activities (MedDRA) terms. AEs were defined and graded according to the Common Terminology Criteria for Adverse Events (CTCAE) version 3.0. The category, severity, and relationship of the AE to the treatment protocol were tabulated. Serious AEs (SAEs) were listed separately. The incidence and severity of OHSS, the proportion of cycles cancelled due to OHSS, and the incidence of multiple pregnancies were noted. The criteria used for grading of OHSS are shown in Supplementary Table S4.

Statistical analysis

Data were analyzed using SAS 9.3. Continuous data are reported as the mean ± standard deviation (SD). Categorical data are presented as the number of cases and frequency (%). Prior to statistical comparisons, normality tests were used to determine whether the data were normally distributed. Intergroup comparisons of normally distributed continuous data were made using one-way analysis of variance (ANOVA). Intergroup comparisons of non-normally distributed continuous data were made using the Kruskal-Wallis non-parametric method. Intergroup comparisons of binary variables (e.g., implantation rate and pregnancy rates) were performed using the chi-squared test.

Results

Enrollment of the study subjects

Of the 801 subjects initially enrolled in the study, 27 (3.4 %) were subsequently excluded due to violation of exclusion criteria and/or lack of BMI measurement; therefore, 774 subjects were included in the analysis (Fig. 1).

Baseline characteristics and distribution of BMI categories

The baseline demographic and clinical characteristics of the 774 subjects are presented in Table 1. Among the 774 subjects, 51 (6.6 %) were considered underweight, 449 (58.0 %) normal weight, 211 (27.3 %) overweight, and 63 (8.1 %) obese.

The mean duration of infertility was 3.9 ± 2.4 years (range, 1–15 years; $n = 774$; Supplementary Table S5). The most common reasons for infertility (Supplementary Table S5) were PCOS combined with a tubal factor (493/774, 63.7 %), PCOS combined with a male factor (300/774, 38.8 %), and PCOS alone (111/774, 14.3 %). Seven subjects (0.9 %) had

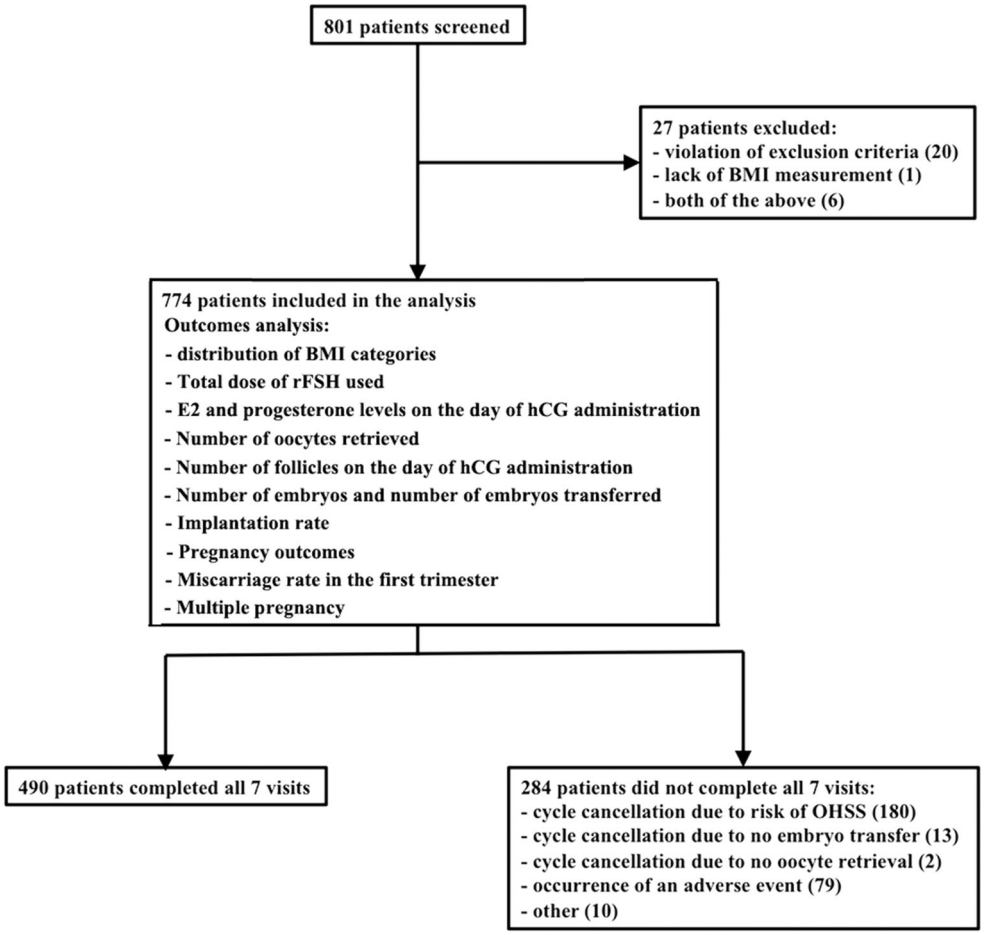

Fig. 1 Patient disposition. *BMI* body mass index, *OHSS* ovarian hyperstimulation syndrome

experienced cycle cancellation in a previous ART treatment (Supplementary Table S5). Baseline testosterone level did not differ significantly among the four BMI categories ($P = 0.286$; Table 1).

Table 1 Baseline demographic and clinical characteristics of the study subjects

	Underweight (BMI <18.5 kg/m^2) ($N = 51$)	Normal weight (BMI 19–23.9 kg/m^2) ($N = 449$)	Overweight (BMI 24–27.9 kg/m^2) ($N = 211$)	Obese (BMI ≥28 kg/m^2 ($N = 63$)	Total ($N = 774$)
Age (years)					
Mean ± standard deviation	26.3 ± 3.1	27.7 ± 3.1	28.5 ± 3.1	28.7 ± 2.7	27.9 ± 3.1
Height (cm)					
Mean ± standard deviation	161.9 ± 5.0	160.6 ± 5.1	160.2 ± 4.8	160.3 ± 5.1	160.6 ± 5.0
Weight (kg)					
Mean ± standard deviation	46.1 ± 3.6	55.0 ± 5.1	66.0 ± 5.0	78.8 ± 7.3	59.4 ± 9.6
BMI (kg/m^2)					
Mean ± standard deviation	17.6 ± 0.8	21.3 ± 1.4	25.7 ± 1.1	30.7 ± 2.4	23.0 ± 3.5
Basal testosterone level (ng/mL)					
Median (interquartile range)	0.40 (0.30–0.50)	0.40 (0.30–0.50)	0.50 (0.30–0.60)	0.40 (0.30–0.60)	0.40 (0.30–0.60)
Total dose of rFSH administered (IU)	$n = 51$	$n = 449$	$n = 211$	$n = 63$	$n = 774$
Mean ± standard deviation	1288 ± 335	1357 ± 375	1646 ± 501	1746 ± 503	1463 ± 449
Estradiol level on hCG day (pg/mL)	$n = 50$	$n = 446$	$n = 210$	$n = 63$	$n = 769$
Mean ± standard deviation	6222 ± 2817	5985 ± 2725	4860 ± 2602	5193 ± 2960	5629 ± 2763
Progesterone level on hCG day (ng/mL)	$n = 50$	$n = 448$	$n = 209$	$n = 62$	$n = 770$
Mean ± standard deviation	1.20 ± 0.70	1.00 ± 0.51	1.00 ± 0.74	0.90 ± 0.48	1.00 ± 0.59

BMI body mass index, *hCG* human chorionic gonadotropin

Comparisons among the four BMI categories revealed that the total dose of rFSH used differed significantly among the categories ($P < 0.001$) and was higher in the obese category than in the underweight category (1746 ± 503 vs 1288 ± 335 IU) (Table 1). There were no statistically significant differences among the BMI categories in the number of oocytes retrieved ($P = 0.075$; Table 2). There was a significant difference among the BMI categories in the number of follicles of diameter 14–18 mm ($P = 0.002$; Table 2). Furthermore, subjects in the normal-weight category had numerically the highest number of follicles of diameter 14–18 mm (Table 2). There was no significant difference among the BMI categories in the number of embryos ($P = 0.577$; Table 2) and number of embryos transferred ($P = 0.820$; Table 2).

Implantation rate and pregnancy outcomes

The mean implantation rate for all patients was 43.0 %. Subjects in the obese category had a lower implantation rate than subjects in the normal-weight category (25.3 vs 45.7 %). The biochemical pregnancy rate, clinical pregnancy rate, and ongoing pregnancy rate per stimulation cycle were 42.2 % (326/773), 34.9 % (270/773), and 28.8 % (223/773), respectively (Table 3). There was no significant difference in the clinical pregnancy rate ($P = 0.132$) and ongoing pregnancy rate ($P = 0.314$) per stimulation cycle among the different BMI categories (Table 3), but the biochemical pregnancy rate per stimulation cycle differed among the various BMI categories ($P = 0.025$; Table 3). The miscarriage rate in the first trimester was 2.2 % (17/774), 3.9 % (2/51) in the underweight category, 1.6 % (7/449) in the normal weight category, 3.8 % (8/211) in the overweight category, and 0 % (0/63) in the obese category. The incidence of multiple pregnancy was 9.9 % (78/791); 77/791 (9.7 %) were twin pregnancies.

Adverse events

A total of 791 subjects (98.8 %) received at least one dose of rFSH and were included for analysis in the safety population. Among these, 378 subjects (47.8 %) experienced at least one AE during the study, and study treatment-related AEs occurred in 161 subjects (20.4 %). During the study period, 26 subjects (3.3 %) experienced SAEs, 6 (0.8 %) of which were judged by the investigator to be related to the study treatment. There was no death.

As shown in Table 4, the most frequent AEs during the study were OHSS, including risk of OHSS (190/791, 24.0 %) and occurrence of OHSS (93/791, 11.8 %) and ectopic pregnancy (12/791, 1.5 %). The incidence of other AEs was <1 % (Table 4 and Supplementary Table S6).

The SAEs are detailed in Table 4 and included OHSS (15/791, 1.9 %), ectopic pregnancy (6/791, 0.8 %), threatened

Table 2 Number of oocytes retrieved, number of follicles on hCG day, number of embryos, and number of embryos transferred

	Underweight (BMI <18.5 kg/m^2) ($N = 51$)	Normal weight (BMI 19–23.9 kg/m^2) ($N = 449$)	Overweight (BMI 24–27.9 kg/m^2) ($N = 211$)	Obese (BMI ≥28 kg/m^2) ($N = 63$)	Total ($N = 774$)
Number of oocytes retrieved[a]	$n = 51$	$n = 448$	$n = 211$	$n = 63$	$n = 773$
Mean ± standard deviation	17.2 ± 7.9	17.4 ± 7.1	15.9 ± 7.7	16.0 ± 8.1	16.9 ± 7.5
Number of follicles <14 mm in diameter[b]	$n = 46$	$n = 433$	$n = 197$	$n = 63$	$n = 739$
Mean ± standard deviation	6.50 ± 6.10	7.10 ± 6.71	7.70 ± 6.87	7.50 ± 6.83	7.20 ± 6.72
Number of follicles of diameter 14–18 mm[c]	$n = 46$	$n = 433$	$n = 197$	$n = 63$	$n = 739$
Mean ± standard deviation	6.40 ± 3.84	8.10 ± 4.89	7.00 ± 4.17	6.80 ± 3.77	7.60 ± 4.60
Number of follicles >18 mm in diameter[d]	$n = 50$	$n = 442$	$n = 210$	$n = 63$	$n = 765$
Mean ± standard deviation	8.40 ± 4.38	7.70 ± 4.08	7.50 ± 4.72	7.70 ± 4.26	8.60 ± 4.52
Number of embryos[e]	$n = 51$	$n = 445$	$n = 211$	$n = 63$	$n = 770$
Mean ± standard deviation	6.70 ± 4.55	7.60 ± 4.60	7.40 ± 5.30	7.50 ± 5.28	7.50 ± 4.85
Number of embryos transferred[f]	$n = 38$	$n = 254$	$n = 144$	$n = 45$	$n = 481$
Mean ± standard deviation	1.90 ± 0.31	1.90 ± 0.32	1.9 ± 0.34	1.90 ± 0.25	1.90 ± 0.32

BMI body mass index, *hCG* human chorionic gonadotropin

[a] $P = 0.075$, intergroup comparisons using one-way analysis of variance

[b] $P = 0.603$, intergroup comparisons using one-way analysis of variance

[c] $P = 0.002$, intergroup comparisons using one-way analysis of variance

[d] $P = 0.561$, intergroup comparisons using one-way analysis of variance

[e] $P = 0.577$, intergroup comparisons using one-way analysis of variance

[f] $P = 0.820$, intergroup comparisons using one-way analysis of variance

Table 3 Biochemical, clinical, and ongoing pregnancy rates in the study subjects

	Underweight (BMI <18.5 kg/m^2)	Normal weight (BMI 19–23.9 kg/m^2)	Overweight (BMI 24–27.9 kg/m^2)	Obese (BMI ≥28 kg/m^2)	Total
Biochemical pregnancy per stimulation cycle	$n = 51$	$n = 448$	$n = 211$	$n = 63$	$n = 773$
Positive, n (%)[a]	26 (51.0)	170 (37.9)	104 (49.3)	26 (41.3)	326 (42.2)
Clinical pregnancy per stimulation cycle	$n = 51$	$n = 448$	$n = 211$	$n = 63$	$n = 773$
Positive, n (%)[b]	21 (41.2)	150 (33.5)	83 (39.3)	16 (25.4)	270 (34.9)
Ongoing pregnancy per stimulation cycle	$n = 51$	$n = 448$	$n = 211$	$n = 63$	$n = 773$
Positive, n (%)[c]	17 (33.3)	126 (28.1)	67 (31.8)	13 (20.6)	223 (28.8)
Biochemical pregnancy per transferred cycle	$n = 38$	$n = 254$	$n = 144$	$n = 45$	$n = 481$
Positive, n (%)[d]	26 (68.4)	170 (66.9)	104 (72.2)	26 (57.8)	326 (67.8)
Clinical pregnancy per transferred cycle	$n = 38$	$n = 254$	$n = 144$	$n = 45$	$n = 481$
Positive, n (%)[e]	21 (55.3)	150 (59.1)	83 (57.6)	16 (35.6)	270 (56.1)
Ongoing pregnancy per transferred cycle	$n = 38$	$n = 254$	$n = 144$	$n = 45$	$n = 481$
Positive, n (%)[f]	17 (44.7)	126 (49.6)	67 (46.5)	13 (28.9)	223 (46.4)

BMI body mass index, *hCG* human chorionic gonadotropin

[a] $P = 0.025$, intergroup comparisons using one-way analysis of variance

[b] $P = 0.132$, intergroup comparisons using one-way analysis of variance

[c] $P = 0.314$, intergroup comparisons using one-way analysis of variance

[d] $P = 0.327$, intergroup comparisons using one-way analysis of variance

[e] $P = 0.033$, intergroup comparisons using one-way analysis of variance

[f] $P = 0.084$, intergroup comparisons using one-way analysis of variance

abortion (3/791, 0.4 %), urinary retention (1/791, 0.1 %), and ovarian torsion (1/791, 0.1 %). The study treatment-related SAEs consisted of OHSS in six subjects (0.8 %): one in the underweight category and five in the normal weight category.

The risk of OHSS and occurrence of OHSS were reported in 190 (24.0 %) and 93 (11.8 %) subjects, respectively (Supplementary Table S6). Most occurrences of OHSS were considered to be mild or moderate in intensity (Supplementary Table S6).

The rate of cycle cancellation due to risk of OHSS was 17.6 % (9/51) in the underweight category, 27.8 % (128/460) in the normal-weight category, 13.4 % (29/216) in the overweight category, 21.9 % (14/64) in the obese category, and 22.8 % (180/791) in the safety population overall.

Discussion

The main findings of the present study were that more than one third of Chinese women with PCOS undergoing IVF/ICSI have a BMI above the normal range, with 27.3 % overweight and 8.1 % obese. The rFSH requirement in the obese category was higher than that in the underweight category. An elevated BMI in women with PCOS was associated with fewer follicles of 14–18 mm in diameter and lower rates of implantation, biochemical pregnancy (per stimulation cycle), and clinical pregnancy (per transferred cycle), but without difference on the rate of ongoing pregnancy.

Some previous investigations have concluded that there may be an optimal body weight for reproductive function in women, with an increased risk of anovulatory infertility both in underweight and overweight/obese women [12]. Reduced fecundity in underweight and overweight women might be related to multiple endocrine, adipokine, and metabolic alterations that affect follicle growth, embryo development, and implantation [13–15]. In women without PCOS, there is evidence that estradiol levels may decrease with increasing BMI [16–21]. However, in our cohort of women with PCOS, there were no obvious differences among the various BMI categories in the levels of estradiol and progesterone on the hCG day or in the baseline testosterone levels.

We determined that 35.4 % (274/774) of our study subjects were overweight or obese, similar to values of 38.3 % (49/128) and 40.6 % (279/688) obtained in previous studies of women with PCOS [22, 23]. Most previous investigations have reported that elevated BMI is associated with the requirement for higher total dose (and/or duration) of gonadotropin, both in women with PCOS [22] and in those without PCOS [14, 16–18, 24–30], supporting the present study.

We observed no differences among BMI categories in the number of follicles retrieved, number of embryos, and number of embryos transferred, which are supported by studies in women with PCOS [22] and without PCOS [19, 27, 28, 31–36], but this is controversial [14, 21, 29, 30, 37]. Interestingly, we found that women of normal weight had more follicles of 14–18 mm in diameter than

Table 4 Adverse events

	Underweight (BMI <18.5 kg/m^2) (N = 51)	Normal weight (BMI 19–23.9 kg/m^2) (N = 460)	Overweight (BMI 24–27.9 kg/m^2) (N = 216)	Obese (BMI ≥28 kg/m^2) (N = 64)	Total (N = 791)
Adverse events	22 (43.1)	246 (53.5)	87 (40.3)	23 (35.9)	378 (47.8)
Gastrointestinal disorders	2 (3.9)	3 (0.7)	1 (0.5)	0 (0.0)	6 (0.8)
Abdominal pain	1 (2.0)	3 (0.7)	1 (0.5)	0 (0.0)	5 (0.6)
Constipation	1 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
Hepatobiliary disorders	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)
Hepatic function abnormal	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)
Pregnancy, puerperium and perinatal conditions	8 (15.7)	56 (12.2)	24 (11.1)	5 (7.8)	93 (11.8)
Abortion	1 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
Abortion threatened	0 (0.0)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.4)
Ectopic pregnancy	0 (0.0)	6 (1.3)	5 (2.3)	1 (1.6)	12 (1.5)
Renal and urinary disorders	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.6)	1 (0.1)
Urinary retention	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.6)	1 (0.1)
Reproductive system and breast disorders	13 (25.5)	194 (42.2)	62 (28.7)	18 (28.1)	287 (36.3)
Risk or occurrence of OHSS	13 (25.5)	190 (41.3)	62 (28.7)	18 (28.1)	283 (35.8)
Ovarian torsion	0 (0.0)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.4)
Vaginal hemorrhage	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	2 (0.3)
Treatment-related adverse events	8 (15.7)	105 (22.8)	41 (19.0)	7 (10.9)	161 (20.4)
Gastrointestinal disorders	1 (2.0)	1 (0.2)	0 (0.0)	0 (0.0)	2 (0.3)
Abdominal pain	1 (2.0)	1 (0.2)	0 (0.0)	0 (0.0)	2 (0.3)
Hepatobiliary disorders	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)
Hepatic function abnormal	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)
Pregnancy, puerperium and perinatal conditions	2 (3.9)	5 (1.1)	3 (1.4)	0 (0.0)	10 (1.3)
Twin pregnancy	2 (3.9)	5 (1.1)	3 (1.4)	0 (0.0)	10 (1.3)
Reproductive system and breast disorders	5 (9.8)	98 (21.3)	38 (17.6)	7 (10.9)	148 (18.7)
Risk or occurrence of OHSS	5 (9.8)	97 (21.1)	38 (17.6)	7 (10.9)	147 (18.6)
Ovarian torsion	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)
Serious adverse events	1 (2.0)	18 (3.9)	5 (2.3)	2 (3.1)	26 (3.3)
Pregnancy, puerperium and perinatal conditions	0 (0.0)	7 (1.5)	3 (1.4)	0 (0.0)	10 (1.3)
Abortion threatened	0 (0.0)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.4)
Ectopic pregnancy	0 (0.0)	4 (0.9)	2 (0.9)	0 (0.0)	6 (0.8)
Renal and urinary disorders	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.6)	1 (0.1)
Urinary retention	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.6)	1 (0.1)
Reproductive system and breast disorders	1 (2.0)	12 (2.6)	2 (0.9)	1 (1.6)	16 (2.0)
Risk or occurrence of OHSS	1 (2.0)	11 (2.4)	2 (0.9)	1 (1.6)	15 (1.9)
Ovarian torsion	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)

Data presented as *n* (%)

BMI body mass index, *OHSS* ovarian hyperstimulation syndrome

subjects in other BMI categories, which is supported by a previous observation that PCOS and obesity independently influence oocyte size [38], and that obesity may be associated with poorer-quality oocytes [20, 28, 30, 39, 40].

A recent study in women with PCOS reported that the implantation rate was lower in overweight/obese subjects than in normal-weight subjects [22, 41], supporting our findings. Provost et al. found that obesity also had a negative impact on IVF outcomes in cycles performed for PCOS [41]. In women without PCOS, some studies have reported a similar effect of elevated BMI on implantation rate [31, 42], whereas others have not [19, 24, 43].

Numerous studies have found a significant effect of elevated BMI on pregnancy rates [20, 26, 28, 29, 31, 36, 44–46], whereas several others have determined no such effect [18, 19, 21, 22, 24, 27, 30, 32–35, 39, 47, 48]. In a recent study,

women with a BMI <24 kg/m^2 had a higher clinical pregnancy rate than those with a BMI ≥24 kg/m^2 [23], supporting our findings. In addition, in the present study, the miscarriage rates were not significantly different among the various BMI categories, which is supported by previous studies [14, 16, 26, 49, 50], but this is controversial [19, 30, 35, 47]. Notably, another study in Chinese women with PCOS concurred with our findings [23].

Nearly half of all subjects experienced at least one AE. The most common AEs were OHSS and ectopic pregnancy. The incidence of OHSS observed in Chinese women with PCOS in this study (11.8 %) was similar to that reported by a previous study (10 %) [25], but notably higher than that in the general population of women undergoing IVF/ICSI (2.9–6.5 %) [18, 19, 51, 52].

In the present study, there was no obvious effect of BMI on OHSS, which is supported by previous studies [18, 19, 25, 51, 52]. The present study suggests that BMI does not influence the incidence of OHSS or the rate of cycle cancellation. Our results were consistent with several previous investigations in women without PCOS that have reported no effect of BMI on cycle cancellation, although there is also more limited evidence that elevated BMI may enhance the rate of cycle cancellation [16, 21]. Overall, this would suggest that although PCOS is an important risk factor for OHSS and thus cycle cancellation, BMI is unlikely to mediate this effect since BMI itself appears to have little or no direct influence on the incidence of OHSS or the rate of cycle cancellation due to OHSS. Further studies are needed to clarify the mechanisms by which PCOS promotes the occurrence of OHSS after IVF/ICSI.

This observational study has several limitations. First, as this was not an interventional study, it was not possible to determine whether BMI reduction would be associated with reduced rFSH requirements and improved clinical pregnancy rate; thus, causality could not be established. Second, selection bias cannot be ruled out because of the age limit. Third, it cannot be excluded that one or more confounding factors, rather than BMI itself, were responsible for the observed differences in outcome. In addition, each center was allowed to use their local COH protocol, and GnRH antagonist regimens were not widely recognized in China before 2012 [53] (the present study was designed in 2011). No data were available on the morphology of the transferred embryos. Finally, this study aimed to examine the impact of BMI on pregnancy outcome of women with PCOS undergoing IVF/ICSI, but it is likely that overweight and obese women received higher doses of rFSH because of excess weight. Additional studies are needed to further characterize the influence of BMI on pregnancy outcomes in Chinese women with PCOS undergoing IVF/ICSI.

In conclusion, the present study suggests that more than one third of Chinese women with PCOS undergoing IVF/ICSI were overweight or obese. Furthermore, elevated BMI was associated with reduced clinical pregnancy rate but similar ongoing pregnancy rates, suggesting that BMI ultimately has a low impact on IVF outcomes. Further studies are needed to confirm and expand on our observations and to determine whether elevated BMI in women with PCOS affects longer-term pregnancy outcomes (such as live birth rate).

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The study was approved by the ethics committees of the participating hospitals.

Informed consent All study subjects were fully informed as to the nature of the study and provided written consent for inclusion.

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