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Effect of body mass index on pregnancy outcomes in young women with low-prognosis POSEIDON criteria after in vitro fertilization/ intracytoplasmic sperm injection

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Abstract

Background The aim of this study was to investeigate the pregnancy outcomes of young women with low prognosis according to the POSEIDON criteria after IVF/ICSI cycles and to explore the effect of body mass index (BMI) on pregnancy outcomes.

Methods This was a retrospective cohort study conducted in women who underwent their first IVF/ICSI cycle treatment between January 2018 and December 2020, Among them, these patients who met criteria for POSEIDON group1and 3 were further categorized into four groups according to the China body mass index(BMI) classification, we analyzed the effect of BMI on pregnancy outcomes.

Results A total of 29,354 patients were conducted first IVF/ICSI cycle between January 2018 and December 2020 in our reproductive center, 5981 women who met the criteria for POSEIDON 1 and POSEIDON 3 were further categorized into four groups according to the China body mass index(BMI) classification. There were not significant differences in the implantation rate and clinical pregnancy rate, regardless of fresh embryo transfer or frozen embryo transfer among the four groups ($P > 0.05$). The miscarriage rate of fresh embryo transfer was significantly higher in obese patients ($P < 0.05$), while the live birth rate of fresh embryo transfer and the cumulative live birth rate are significantly lower in obese patients($P < 0.05$). BMI was a significant and independent predictor of the miscarriage rate of fresh embryo transfer (adjusted OR 1.111; 95% CI 1.042–1.184; $p = 0.001$) and the cumulative live-birth rate (adjusted OR 0.937; 95% CI 0.900–0.975; $p = 0.001$).

Conclusions Our study indicated that obesity negatively impacts the IVF/ICSI outcomes of young women with low prognosis, including higher miscarriage rate and lower live birth-rate and cumulative live-birth rate. In our study, we found that BMI was the best independent predictor of the miscarriage rate of fresh embryo transfer and cumulative live-birth rate of low-prognosis patients under 35 years old. Thus the best way to reduce these complications for young patients with a poor prognosis was to keep their BMI between 18.5 kg/m^2 and 24 kg/m^2.

Keywords Body Mass Index, POSEIDON criteria, Pregnancy Outcomes, In Vitro Fertilization/IntraCytoplasmic Sperm Injection

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Introduction

It is well known that there is still a long way to go for the medical management of patients with a poor prognosis. Alviggi et al. proposed the POSEIDON criteria in 2016 [1], following the Bologna criteria in 2011 [2]. Several studies have addressed the issue that an increase in female age is associated with fewer euploid embryos [3] and more implantation failure, especially for women over 35 years old. Therefore, age is a dominant factor in a successful pregnancy and a healthy baby, and the age of women is the main factor in giving birth. It is another point of confusion for clinicians that large numbers of women with obesity who are undergoing in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI) have shown more difficulties related to body mass index (BMI, kg/m^2), in addition to age. A recent study has shown that the risk ratio of infertility is 1.18 [95% confidence interval (CI): 1.05–1.31] per 1-unit increment of BMI when BMI exceeds 30 kg/m^2 [4]. Many trials have revealed a progressive impairment of in vitro fertilization (IVF) outcome in women with obesity, including poorer implantation, clinical pregnancy, live birth, and higher miscarriage rates, compared with normal-BMI patients [5, 6]. However, few studies have explored the impact of BMI among low-prognosis patients undergoing IVF. Thus, the objective of our study is to evaluate the effect of BMI on IVF outcomes in a large cohort of young women with low prognosis undergoing IVF/ICSI cycles.

Methods

Study design and population

This retrospective cohort study was approved by the ethics committee of the Peking University Third Hospital. All young low-prognosis patients who underwent their first IVF/ICSI treatments during the period from January 2018 to December 2020 were enrolled. Young low-prognosis was defined according to the POSEIDON criteria Group 1 and Group 3 (age < 35 years old, number of oocytes retrieved ≤ 9, used standard ovarian stimulation protocols). The exclusion criteria were as follows: (1)age ≥ 35 years old, (2)chromosomal abnormality, (3) preimplantation genetic testing (PGT) cycles, (4)uterine malformations, (5)using non-standard ovarian stimulation protocol and (6)fertility preservation. Young low-prognosis patients were further categorized into four groups according to the China BMI classification [7], namely, underweight (BMI < 18.5 kg/m^2), normal weight (18.5 ≤ BMI < 24 kg/m^2), overweight (24 ≤ BMI < 28 kg/m^2), and obese (BMI ≥ 28 kg/m^2). A flowchart of the patient selection process is presented in Fig. 1.

Clinical settings

Patients accepted standard ovarian stimulation protocols, such as long gonadotropin-releasing hormone (GnRH) agonist and antagonist protocols. Ovarian stimulation regimen and dosage of gonadotropins selection was based on female age、BMI、 AMH、AFC and other characteristics by experienced physicians. Once two or three follicles reached a mean diameter of 17 mm, recombiant hCG(250 mg, Ovidrel, Merck)was used to trigger ovulation. Transvaginal oocyte retrieval was performed

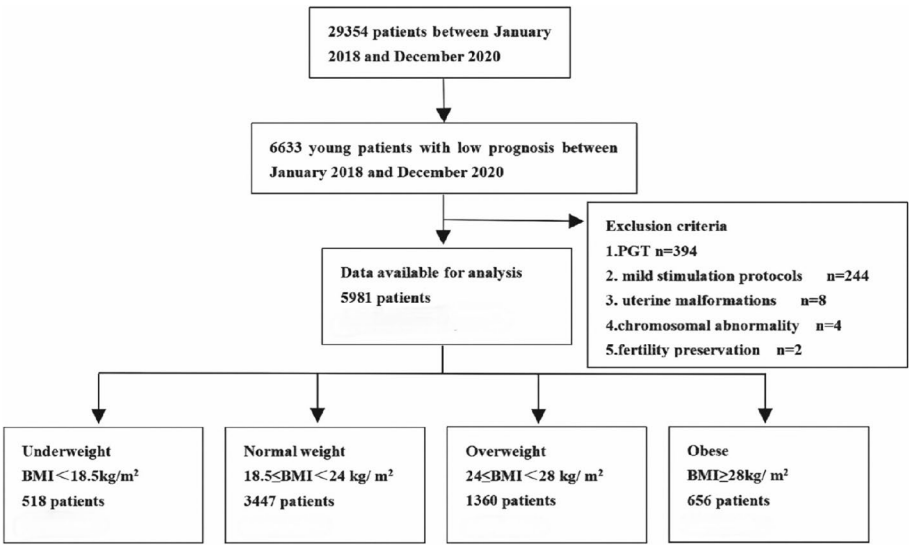

Fig. 1 Study flow chart

with the standard operating procedure 36–38 h after triggering. The collected oocytes were inseminated via IVF or ICSI and then embryos of day 3 or the blastocyst stage were transfered after egg retrieval.. The surplus embryos were vitrified for later frozen embryo transfer(FET) cycles. Progesterone intravaginal gel (Crinone 8% 90 mg/day, Merck-Serono) was provided as support for the luteal phase. The protocol selection of the FET cycle depends on whether the patient' s menstrual cycle is regular or not. In the natural cycle, the endometrium and ovulation were monitored with vaginal ultrasound, and progesterone was administered on the 3rd day after ovulation, followed by embryo transfer, where for day-3 embryos, it was scheduled on the 3rd day after ovulation, or for blastocysts, it was scheduled on the 5th day. In the artificial FET protocol, estradiol valerate (Progynova 4 mg/day, Schering, Berlin, Germany) was supplemented from the 2nd-4th day during menstruation, and the medicine dosage can be adjusted in terms of endometrial thickness. When the endometrial thickness reaches ≥ 8 mm, progesterone administration was initiated and continues for 12 weeks of pregnancy. Embryo transfer was scheduled on the 5th day after luteal support for day-3 embryos or on the 7th day for blastocysts. A blood test for HCG was performed on the 14th day after ET (embryo transfer). A gynecological ultrasound was done to confirm intrauterine pregnancy on the 30th day after ET. Luteal support was discontinued at 8–9 weeks of pregnancy. During the artificial cycle, the medication was gradually reduced starting from the 10th week of pregnancy and completely stopped by the 12th week.

The primary outcome is the cumulative live birth rate (CLBR), defined as the probability of live birth from ovarian stimulation during the study period, including all fresh and frozen embryos transferred from that stimulation. Live birth is classified as the birth of at least one living infant after 28 weeks. The secondary outcome is the rates of implantation, clinical pregnancy, miscarriage, live birth rate (LBR) and characteristics of stimulation procedures, including the number of oocytes retrieved, the number of 2 pro-nucleus (2PN) zygotes and the number of high-quality embryos.

Statistical analysis

All statistical management and analyses were performed using SPSS 25.0 software (IBM Corp., Armonk, NY, USA). One-way analysis of variance (ANOVA) and the post hoc Bonferroni test were used for comparisons of continuous variables between the groups based on the distribution of the data. The chi-square test was used for comparisons of categorical variables, and we also adopted Fisher's exact test if necessary. Continuous variables and categorical variables are represented as the mean ± standard deviation (SD) and frequencies (%), respectively. Logistic regression analysis was used to analyze the elements associated with the miscarriage rate of fresh embryo transfer (ET) and CLBR in the first stimulation cycles; adjusted odds ratios (aORs) and 95% CIs were calculated. A P value of < 0.05 was considered to indicate statistical significance.

Results

A total of 29,354 patients underwent their first IVF/ICSI cycle between January 2018 and December 2020 in our reproductive center, 5981 women met the criteria for POSEIDON 1 and POSEIDON 3 (Fig. 1). In our study, Group 1 included 4,058 individuals, and Group 3 included 1,923 individuals. Baseline characteristics across different BMI groups were described in Table 1. These patients underwent a total of 7543 ET cycles, including fresh ET cycles and FET cycles.

Table 1 showed the baseline characteristics of infertile women among the four BMI categories. Women with normal weight had the highest mean age of all four groups, and the difference was statistically significant ($p = 0.001$), although all the women were under 35 years old. Patients with elevated BMI have increased average infertility duration and antral follicular count (AFC), and the results imply statistical significance ($p < 0.001$). Compared with underweight or normal-weight patients, women in the overweight and obesity categories had higher anti-Müllerian hormone (AMH) levels ($p < 0.001$). The basal serum FSH level decreased with increasing BMI ($p < 0.001$). In the normal weight group, the basal serum E2 level was significantly lower than that in the underweight and obesity groups ($p = 0.001$). Among all BMI categories, the basal serum LH level was the highest in underweight patients ($p < 0.001$). No statistically significant difference was found among the four groups in terms of infertility caused by male factors, tubal factors or other multiple factors. Compared with women in the other BMI categories, women with overweight or obesity have more diagnoses of polycystic ovary syndrome (PCOS)-factor infertility.

Endocrine characteristics and embryology outcomes in the four groups were presented in Table 2. In terms of the controlled ovarian stimulation (COS) cycles, lower starting dosages of gonadotropin (Gn) and longer durations of ovarian stimulation were performed in women who were overweight and obese than in those in the underweight and normal weight groups ($p < 0.05$). There was no significant difference in the total dose of gonadotrophin among the four groups ($p = 0.137$). Compared with the patients with overweight or obesity, women in the underweight and normal-weight categories had higher E2 and P values on the trigger day

Table 1 Baseline characteristics of the patients

	Underweight *n* = 518	Normal weight *n* = 3447	Overweight *n* = 1360	Obese *n* = 656	*P*
Age (years)	30.13 ± 2.76	30.62 ± 2.62	30.36 ± 2.68	30.22 ± 2.78	< 0.001[a,d,e*]
Infertility duration (years)	2.7 ± 1.88	2.96 ± 2.16	3.19 ± 2.15	3.82 ± 2.6	< 0.001[a,b,c,d,e,f]
BMI(kg/m2)	17.58 ± 0.78	21.21 ± 1.48	25.64 ± 1.12	30.54 ± 2.27	< 0.001[a,b,c,d,e,f]
AFC	8.6 ± 4.51	9.31 ± 5.04	10.35 ± 5.64	12.2 ± 6.48	< 0.001[a,b,c,d,e,f]
AMH(ng/ml)	2.29 ± 2.2	2.42 ± 2.57	2.7 ± 2.63	2.9 ± 2.63	< 0.001[b,c,d,e]
Basal serum FSH level (mIU/ml)	8.48 ± 4.17	7.51 ± 3.7	6.99 ± 7.27	6.4 ± 2.38	< 0.001[a,b,c,d,e,f]
Basal serum E2 level (pmol/L)	175.05 ± 78.28	164.4 ± 86.21	166.91 ± 83.29	176.24 ± 83.03	0.001[a,e,f]
Basal serum LH level (mIU/ml)	5.24 ± 13.04	3.97 ± 2.9	3.8 ± 3.9	3.83 ± 3.09	< 0.001[a,b,c]
Infertility cause n (%)					< 0.001
Tubal	205 (39.6)	1333(38.7)	538 (39.6)	235 (35.8)	0.412
Male	149 (28.76)	995 (28.87)	370 (27.21)	156 (23.78)	0.054
Multiple	151 (29.2)	956 (27.7)	333 (24.5)	164 (25.0)	0.051
PCOS	13(2.5)	163(4.7)	119(8.8)	101(15.4)	< 0.001[b,c,d,e,f]

[*] : Data are shown as the number of patients (percentage) or mean ± SD. SD, standard deviation; BMI, body mass index; AMH, anti-Müllerian hormone; AFC, antral follicular count; PCOS, polycystic ovary syndrome; FSH, follicular stimulating hormone E2, estradiol; LH, luteinizing hormone. a $P < 0.05$, underweight vs. normal weight; b $P < 0.05$, underweight vs. overweight; c $P < 0.05$, underweight vs. obese; d $P < 0.05$, normal weight vs. overweight; e $P < 0.05$, normal weight vs. obese; f $P < 0.05$, overweight vs. obese

Table 2 Endocrine characteristics and IVF outcomes

	Underweight *n* = 518	Normal weight *n* = 3447	Overweight *n* = 1360	Obese *n* = 656	*P*
Starting dosage of gonadotropin (IU)	238.88 ± 82.13	233.17 ± 80.33	224.33 ± 77.33	220.2 ± 80.22	< 0.001[b,c,d,e*]
Duration of ovarian stimulation (days)	10.94 ± 2.45	11.12 ± 2.47	11.33 ± 2.6	11.76 ± 2.88	0.017[b,c,d,e,f]
Total dosage of gonadotropin (IU)	2957.57 ± 1335.76	2964.63 ± 1251.04	2924.7 ± 1204.55	3065.31 ± 1355.21	0.137
E2 values on the trigger day (pmol/L)	6701.93 ± 3884.54	5771.36 ± 3180.94	4988.99 ± 2903.51	4737.87 ± 2836.25	< 0.001[a,b,c,d,e]
P values on the trigger day (nmol/L)	2.31 ± 1.34	2.12 ± 4.92	1.72 ± 0.95	1.55 ± 0.78	< 0.001[b,c,d,e]
LH values on the trigger day (mIU/ml)	2.32 ± 4.67	2.35 ± 11.22	2.19 ± 2.78	2.29 ± 2.69	0.952
No. of oocytes retrieved	6.18 ± 2.32	6.24 ± 2.26	6.11 ± 2.24	5.86 ± 2.39	0.001[c,e,f]
No. of 2PN	3.69 ± 2.01	3.67 ± 2.07	3.58 ± 2.06	3.32 ± 2.03	0.001[c,e,f]
No. of high- quality embryos	2.52 ± 1.98	2.56 ± 1.95	2.57 ± 1.93	2.38 ± 1.81	0.169

[*] :Data are shown as the number of mean ± SD. SD, standard deviation; E2, estradiol; LH, luteinizing hormone; P, progesterone; PN, pronucleus. a $P < 0.05$, underweight vs. normal weight; b $P < 0.05$, underweight vs. overweight; c $P < 0.05$, underweight vs. obese; d $P < 0.05$, normal weight vs. overweight; e $P < 0.05$, normal weight vs. obese; f $P < 0.05$, overweight vs. obese

($p < 0.001$), while there were no statistically significant differences in the LH values on the trigger day among groups ($p = 0.952$). In the obese group, the number of oocytes retrieved and 2PN zygotes was the lowest compared to the other three groups ($p = 0.001$). The results showed that no statistically significant differences existed in the numbers of high-quality embryos ($p = 0.169$).

The clinical outcomes of the BMI groups were shown in Table 3. No difference was identified in the implantation rate and clinical pregnancy rate, regardless of whether fresh ET or FET was performed, across all BMI categories ($p > 0.05$). Among all BMI categories, the live birth rate of fresh ET was the highest in underweight patients ($p < 0.05$). The miscarriage rate of fresh ET and live birth rate of fresh ET and FET were the worst in patients with obesity ($p < 0.05$).

Figure 2 demonstrated the multiple logistic regression analysis of the miscarriage rate of fresh ET and the cumulative live birth rate in patients with BMI ≥ 24 kg/m^2. After adjustments for several confounding factors, BMI ≥ 24 kg/m^2 (i.e., women with overweight or obesity) was a significant and independent predictor of the miscarriage rate of fresh ET (aOR 1.111; 95% CI 1.042–1.184; $p = 0.001$) and the cumulative live birth rate (aOR 0.937; 95% CI 0.900–0.975; $p = 0.001$).

Table 4 showed the pregnancy outcomes of PCOS patients, with no significant difference according to BMI

Table 3 Pregnancy outcomes of studied patients

	Underweight n = 518	Normal weight n = 3447	Overweight *n* = 1360	Obese *n* = 656	*P*
Implantation rate of fresh ET n (%)	212 (30.8)	1462 (30.8)	589 (31.7)	257 (28.8)	0.501
Cumulative implantation rate n (%)	288 (33.3)	1885 (32.4)	777 (33.3)	331 (30.9)	0.527
Clinical pregnancy rate of fresh ET n (%)	162 (43.3)	1137 (43.9)	441 (43.7)	202 (40.8)	0.657
Cumulative clinical pregnancy rate n (%)	225 (54.2)	1502 (53.5)	594 (53.6)	261 (49.1)	0.264
Miscarriage rate of fresh ET n (%)	18 (11.1)	145 (12.8)	57 (12.9)	49 (24.3)	< 0.001 [c,e,f*]
Live birth rate of fresh ET n (%)	140 (37.4)	959 (37.0)	373 (36.9)	144 (29.1)	0.007 [a,b,c,e,f]
Cumulative live birth rate n (%)	199 (48.0)	1304 (46.5)	512 (46.2)	196 (36.8)	< 0.001 [c,e,f]

*: Data are shown as the number of patients (percentage). ET, embryo transfer. a $P < 0.05$, underweight vs. normal weight; b $P < 0.05$, underweight vs. overweight; c $P < 0.05$, underweight vs. obese; d $P < 0.05$, normal weight vs. overweight; e $P < 0.05$, normal weight vs. obese; f $P < 0.05$, overweight vs. obese

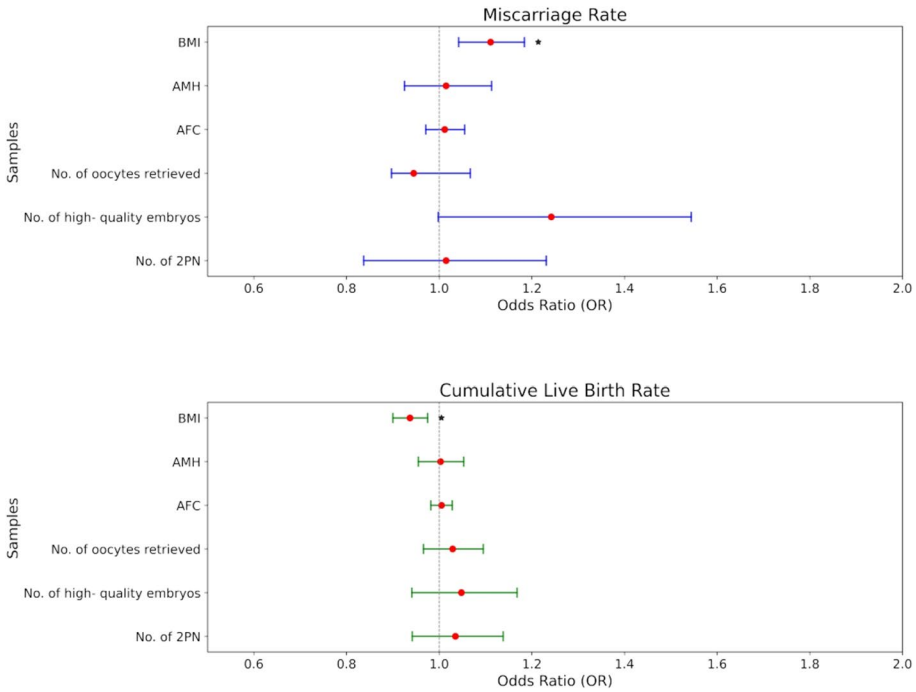

Fig. 2 Multivariate logistic regression analysis of the miscarriage rate of fresh ET and the cumulative live-birth rate

Table 4 Pregnancy outcomes of studied patients with PCOS

	Underweight *n* = 13	Normal weight *n* = 163	Overweight *n* = 119	Obese *n* = 101	*P*
Implantation rate of fresh ET n (%)	2(11.8)	49(22.9)	32(20.8)	31(24.2)	0.656
Cumulative implantation rate n (%)	10(35.7)	79(25.7)	67(30.3)	44(26.5)	0.500
Clinical pregnancy rate of fresh ET n (%)	2(22.2)	43(37.4)	22(26.5)	25(35.2)	0.360
Cumulative clinical pregnancy rate n (%)	6(60.0)	69(50.7)	49(51.8)	36(43.9)	0.650
Miscarriage rate of fresh ET n (%)	0(0)	7(16.3)	3(13.6)	8(32)	0.292
Live birth rate of fresh ET n (%)	2(22.2)	32(27.8)	18(21.7)	14(19.7)	0.594
Cumulative live birth rate n (%)	7(70)	56(41.2)	43(44.8)	25(30.5)	0.051

*: Data are shown as the number of patients (percentage). PCOS, polycystic ovary syndrome; ET, embryo transfer

groups ($p > 0.05$), including implantation rate, clinical pregnancy rate, miscarriage rate and live birth rate.

Table 5 depicted the ovarian function indicators and pregnancy outcomes of non-PCOS studied patients. With increasing BMI, AMH and AFC both increased, while the basal serum FSH level decreased, all of which were statistically significant differences ($p < 0.05$). The pregnancy outcomes were the same as those of the general studied patients: there was no significant difference in the implantation rate and clinical pregnancy rate among the different groups, and compared to the other 3 groups, the miscarriage rate of the obese group was the highest, while the live birth rate was the lowest ($p < 0.05$) regardless of whether fresh ET or FET was performed.

Discussion

This single-center retrospective study demonstrated the impact of the BMI classification on pregnancy outcomes in young(age < 35 years old) POSEIDON patients. While the age was highly related to the aeuploid embryo and live birth outcome, one of the crucial factors in the POSEIDON classification was the female age [8]. Studies explored that there is a significant decrease in clinical pregnancy rate and a significant increase in miscarriage rate by increasing female age and BMI [9–11]. To the best of our knowledge, this was the first study to assess the pregnancy outcomes for young POSEIDON patients according to the BMI classification, to avoid the impact of age-related pregnancy outcomes.

We found that the age of obese group was not the highest, but the duration of infertility was indeed the longest among four BMI categories. Another study also showed the increased time of conception in the obese people [12]. Our study indicated that the number of PCOS was rising with BMI increasing. A recent study illustrated that the risk of PCOS is partly due to the increase of BMI resulting in the dysregulation of the complement system and the concurrent upregulation of its inhibitors [13]. AMH and AFC increases as BMI grows, which might be closely related to the rising proportion of PCOS. In our study, high-quality embryos was not different among four BMI groups, which is similar to other studies [14–16]. Our study showed that the increase of BMI was negatively correlated with basal serum FSH and LH levels, and same as another report [17], which uncovered the obese women have lower FSH and LH levels in the early follicular phase. There was no significant impact of obesity on the ovarian function, suggested by the AFC, AMH and FSH of obese people, possibly because of the increased number of PCOS in obesity women. Among different BMI groups, there was no difference for pregnant outcomes of PCOS patients, including implantation rate, pregnancy rate, miscarriage rate and live birth rate. However, our research indicated the same outcomes for non-PCOS patients – the best ovarian functions remain in the obese people, based on the data from AFC, AMH and FSH of different BMI groups. During the process of COS, the starting dosage of Gn for obese patients was lower than normal weight women and the duration of ovarian stimulation was the longest in obese women compared with other groups. In 2011, two studies pointed out the decrease number of oocytes retrieval in the obese women [18, 19]. These decreased assisted reproductive technologies (ART) outcomes may be related to the decrease trophectoderm cell number and the blastocyst formation with BMI increasing [19].

Although our study showed that no matter it is fresh ET or FET, the implantation rate and clinical pregnancy rate were the worst in obese patients than other groups, there were no statistically significant differences among all BMI

Table 5 Baseline characteristics and pregnancy outcomes of studied patients without PCOS

	Underweight $n=505$	Normal weight $n=3284$	Overweight $n=1241$	Obese $n=555$	*P*
AFC	8.48 ± 4.35	9.08 ± 4.7	9.83 ± 5.24	11.18 ± 6.09	< 0.001 [abcdef*]
AMH (ng/ml)	2.19 ± 2.01	2.28 ± 2.23	2.48 ± 2.42	2.57 ± 2.37	0.003 [bcde]
Basal serum FSH level (mIU/ml)	8.5 ± 4.2	7.52 ± 3.72	7.07 ± 7.58	6.4 ± 2.41	< 0.001 [abcdef]
Implantation rate of fresh ET n (%)	210(31.3)	1413(31.2)	557(32.7)	226(29.6)	0.450
Cumulative implantation rate n (%)	278(33.2)	1806(32.7)	710(33.6)	287(31.7)	0.759
Clinical pregnancy rate of fresh ET n (%)	160(43.8)	1094(44.2)	419(45.2)	177(41.7)	0.700
Cumulative clinical pregnancy rate n (%)	219(54.1)	1433(53.7)	545(53.8)	225(50.0)	0.514
Miscarriage rate of fresh ET n (%)	18(11.3)	138(12.6)	54(12.6)	41(23.2)	0.001 [cef]
Live birth rate of fresh ET n (%)	138(37.8)	927(37.4)	355(38.3)	130(30.7)	0.041 [abcef]
Cumulative live birth rate n (%)	192(47.4)	1248(46.7)	469(46.3)	171(38.0)	0.006 [cef]

[*]: Data are shown as the number of patients (percentage) or mean ± SD. SD, standard deviation; PCOS, polycystic ovary syndrome; AFC, antral follicular count; AMH, anti-Müllerian hormone; FSH, follicular stimulating hormone. a $P < 0.05$, underweight vs. normal weight; b $P < 0.05$, underweight vs. overweight; c $P < 0.05$, underweight vs. obese; d $P < 0.05$, normal weight vs. overweight; e $P < 0.05$, normal weight vs. obese; f $P < 0.05$, overweight vs. obese

groups. These findings were inconsistent with three previous studies [5, 6, 9]. The variance might be caused by no statistically significant differences in the number of high-quality embryos among groups in our study with low prognosis patients. A recent meta-analysis found the similar result [20]. The mechanisms of obesity effects on oocyte and embryos developments are complex. The accumulated fats were associated with a higher prevalence of mitochondrial dysfunction and insulin resistance in the body [21, 22], which causes spindle anomalies, chromosome segregation, and oocyte development [23]. A neurotransmitter peptide named NPY stimulated fat angiogenesis and proliferation via kisspeptin cells [24] and it also promoted appetite [25]. Meanwhile, NPY impaired follicle development though a promoting apoptosis and anti-proliferation effect [26]. However, previous experiments reported that there is no statistical difference in the proportion of euploid embryos among different BMI groups [27, 28], where the results are similar to our analysis.

A recent predictive model based on the research [29] of low prognosis patients with pregnancy failure pointed out that the low prognosis patients experiencing pregnancy failure is related to BMI > 24 kg/m2, which is different from our results. Although the implantation rate of obese group was the worst in our research, there was no statistical differences among different BMI groups, where the reason might be the elimination of the key factor for the pregnancy outcomes – age. Miscarriage rate was apparently worst in patients with obesity as shown in our study. Multiple researches suggested a relationship between obesity and increased miscarriage rate [30, 31]. We found live birth rate was the worst in the obese women, no matter fresh ET or FET. Similarly, a meta-analysis indicate that the increase of BMI is associated with worse live birth rate [32, 33]. Compared with normal weight women, the obese women have better ovarian function (higher AFC, AMH and lower FSH), as well as the similar number of high-quality embryos, the percentage of implantation and clinical pregnancy, but miscarriage rate was higher and live birth rate was lower. A time-lapse study including 7180 embryos reported that obese women's embryos had cleavage delayed compared with normal weight women [34]. Two studies showed that the effect of obesity on fatty acid composition and concentration may have an effect on embryo function [14, 15]. Several studies suggested a number of obesity-related factors, such as endometrial gene expression, hormone receptor expression patterns, proteomic analysis of the endometrium, leptin and pro-inflammatory markers [35–39], increase the miscarriage risk. Meanwhile, these factors might also possibly increase the risk of pregnancy complications such as pre-eclampsia, gestational diabetes and pro-longed duration of labor, shoulder dystocia, caesarean delivery, macrosomia, and increased blood loss [6, 40–42] Our research showed that the increasing of risks of the miscarriage caused by obesity may lower the cumulative live birth rate. It is complex for the mechanisms of how obesity influences younger women with low prognosis reproductive function. A study implied that the lipids and the inflammatory markers caused by obesity in the follicular fluid impair the follicle development [43], leading to the increasing impairment in low prognosis patients.

Our results suggested that the miscarriage rate of fresh ET increases 11.1% and cumulative live birth rate decreases 6.3% for each additional BMI unit when BMI exceeds 24 kg/m2. Although the standards of BMI research vary among previous studies, BMI was an independent risk factor of miscarriage rate for the overweight and obese patients. Recent research[44] of predictive factors for POSEIDON patients' pregnancy outcomes showed a negative relation between BMI and live birth rate (OR 0.9; 95% CI 0.9–1.0; $p < 0.001$) for BMI ≤ 23.4 kg/m2, but for BMI > 23.4 kg/m2, it shows a non-significant relation (OR 1.0; 95% CI 0.9–1.1; $p = 0.999$), which is different from our research. Different BMI standards and research people might contribute to the different research results between us. Our research targets more on the younger women with low prognosis. Thus, reducing weight may reduce these complications for the younger POSEIDON patients with high BMI. However, 3 randomized trials[45–47] in recent years showed no better pregnant outcomes for infertile obese patients losing weights before pregnancy.

The drawbacks in our current research: the primary one is the inherent limitations of retrospective study. Inconsistent COS protocol might affect the number of oocytes retrieved, which further influence the finalization of low prognosis patients. Furthermore, due to the time limitation, we cannot follow the research of all the FET cycles after the first time of IVF.

Conclusions

Our study indicates that the obesity negatively impacts IVF/ICSI outcomes of younger women with low prognosis, especially for the stage after implantation, including the miscarriage rate, live birth rate and cumulative live birth rate. BMI is the best independent predictor of the miscarriage rate of fresh ET and CLBR for low prognosis patients under 35 years old. The effects of obesity on younger women with low prognosis still need to be required by large sample size and prospective research.

Abbreviations

BMI	Body mass index
IVF/ICSI	In vitro fertilization/intracytoplasmic sperm injection

ET	Embryo transfer
PGT	Preimplantation genetic testing
GnRH	Gonadotropin-releasing hormone
FET	Frozen embryo transfer
CLBR	Cumulative live birth rate
LBR	Live birth rate
2PN	2 Pro-nucleus
ANOVA	One-way analysis of variance
SD	Standard deviation
aORs	Adjusted odds ratios
AFC	Antral follicular count
AMH	Anti-Müllerian hormone
PCOS	Polycystic ovary syndrome
COS	Controlled ovarian stimulation
Gn	Gonadotropin
ART	Assisted reproductive technologies

Supplementary Information

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Supplementary Material 1.

Supplementary Material 2.

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Authors' contributions
Xiumei Zhen, Yiting Ren, Rong Li and Lina Wang devised this research, collect the data, and analyze the results. Chen Yang and Tian Tian participated in the data statistics.

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Data Availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
This retrospective cohort study was approved by the ethics committee of the Peking University Third Hospital.A statement confirming that the Ethics Committee is organized and operates according to Good Clinical Practice which is pass ed by NMPA and National Health Commission of the people's Republic of China, ICH-GCP, Biomedical Research Ethics Review involving human which is passed by National Health Commission of the people's Republic of China, Helsinki Declaration and ethical principles of International ethical guidelines for biomedical research involving human subjects which is passed by Council for International Organizations of Medical Science (CIOMS).
The name of the ethics committee: Peking University Third Hospital Medical Science Research Ethics Committee.
The committee's reference number: IRB00006761-M2022261.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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