

Effect of different combinations of serum antimüllerian hormone levels and body mass index on pregnancy outcomes in women with polycystic ovary syndrome



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The authors report no conflict of interest.

All the participants gave their written informed consent.

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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BACKGROUND: Both antimüllerian hormone and body mass index are associated with the pregnancy outcomes in women with polycystic ovary syndrome undergoing in vitro fertilization.

OBJECTIVE: This study aimed to explore the effect of different combinations of antimüllerian hormone and body mass index on pregnancy outcomes in women with polycystic ovary syndrome undergoing in vitro fertilization.

STUDY DESIGN: This was a post hoc secondary analysis of a multicenter randomized trial. A total of 625 women from 1 center with antimüllerian hormone levels measured before in vitro fertilization treatment were classified into 6 groups: group A (normal weight and low antimüllerian hormone group), group B (normal weight and intermediate antimüllerian hormone group), group C (normal weight and high antimüllerian hormone group), group D (overweight/obese and low antimüllerian hormone group), group E (overweight/obese and intermediate antimüllerian hormone group), and group F (overweight/obese and high antimüllerian hormone group).

RESULTS: After adjustment via multivariate logistic regression, the overweight/obese and high antimüllerian hormone group (group F) had a higher risk of clinical pregnancy miscarriage (adjusted odds ratio, 3.30; 95% confidence interval, 1.35–8.07) than the normal weight and intermediate antimüllerian hormone group (group B). Both the normal weight and high antimüllerian hormone group (group C; adjusted odds ratio, 3.74; 95% confidence interval, 1.06–13.24) and the overweight/obese and high antimüllerian hormone group (group F; adjusted odds ratio, 3.61; 95% confidence interval, 1.05–12.38) had higher risks of ovarian hyperstimulation syndrome than the normal weight and intermediate antimüllerian hormone group (group B).

CONCLUSION: In women with polycystic ovary syndrome, high serum antimüllerian hormone levels were associated with an increased risk of clinical pregnancy miscarriage in women who were overweight/obese but not in those with normal weight.

Key words: antimüllerian hormone, body mass index, clinical pregnancy miscarriage, ovarian hyperstimulation syndrome, polycystic ovary syndrome

Introduction

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in reproductive-age women and is characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology.¹ In addition to the 3 main characteristics, serum levels of antimüllerian hormone (AMH) are significantly increased in women with PCOS than in ovulatory women,^{2–4} possibly because of the increased antral follicles

and overproduction of AMH by granulosa cells.^{5,6} According to the 2023 international evidence-based guidelines for PCOS, AMH levels serve as an alternative to antral follicle count (AFC) as one of the diagnostic criteria for PCOS.⁷ Moreover, women with PCOS frequently display metabolic comorbidities,⁸ and many women with PCOS are overweight or obese.⁹

It has been suggested that AMH and body mass index (BMI) are separately

AJOG Global Reports at a Glance

Why was this study conducted?

Although much is known about the separate effects of antimüllerian hormone (AMH) and body mass index (BMI) on pregnancy outcomes in women with polycystic ovary syndrome (PCOS), limited information is available regarding the different combinations of serum AMH levels and BMI on pregnancy outcomes in women with PCOS undergoing in vitro fertilization (IVF).

Key findings

In women with PCOS, high serum AMH levels were associated with an increased risk of clinical pregnancy miscarriage in women who were overweight/obese but not in those with normal weight. A high serum AMH level was associated with a high risk of ovarian hyperstimulation syndrome (OHSS), regardless of BMI in women with PCOS.

What does this add to what is known?

Our study suggests that BMI-stratified AMH analysis facilitates the identification of high-risk populations for clinical miscarriages in women with PCOS. Extra caution is required in the clinical management of IVF in women who are overweight/obese and have high AMH levels.

associated with disease severity and pregnancy outcomes in women with PCOS.^{10,11} Women with high serum AMH levels are usually characterized by increased rates of amenorrhea, hyperandrogenism, and polycystic ovarian morphology.^{12,13} A high serum concentration of AMH has been reported to be associated with a lower rate of live birth¹⁴ and an increased risk of preterm delivery^{15,16} in women with PCOS who conceived from in vitro fertilization (IVF) treatment. Studies have shown that women with PCOS with higher levels of AMH are associated with a higher ovarian response and an increased risk of ovarian hyperstimulation syndrome (OHSS).^{17,18} However, BMI is negatively associated with the number of oocytes retrieved, peak estrogen levels, and the risk of OHSS when examining the effect of overweight/obesity alone on ovarian responsiveness.^{19,20} Overweight/obesity exacerbates many aspects of the manifestation of PCOS, including abnormal cardiometabolic function (such as hypertension, glucose intolerance, and dyslipidemia), infertility, and reduced efficacy of fertility treatments.^{21–23} Because of the heterogeneity in PCOS, patients may have varied combinations of AMH levels and BMI. It remains unclear how the combination of these 2 factors affects

the ovarian response and pregnancy outcomes in patients with PCOS.

Several studies have investigated the correlation between AMH and BMI in women with PCOS, with controversial conclusions.^{2,24–29} Although some studies have shown that BMI is adversely associated with serum AMH levels,^{26–29} other studies have found no significant correlation between AMH and BMI.^{2,24,25} It has been suggested that the reference value of AMH for diagnosing PCOS varies among different BMI range categories, and the combined analysis of AMH and BMI facilitates the diagnosis of PCOS.^{27,28}

PCOS accounts for 80% of anovulatory infertility cases.³⁰ IVF treatment is commonly used in women with PCOS who fail to conceive with ovulation induction or who have concomitant infertility factors. However, even when women successfully conceive, they are confronted with increased risks of adverse outcomes, such as OHSS, pregnancy loss, preterm delivery, gestational diabetes mellitus (GDM), and preeclampsia.^{31–34} Further studies are needed to investigate the combined effects of BMI and AMH on pregnancy outcomes and maternal and neonatal complications. We previously conducted a multicenter randomized trial comparing elective frozen embryo

transfer and fresh embryo transfer in 1508 patients with PCOS (Frefro-PCOS), during which the data on AMH and BMI before ovarian stimulation for 625 patients were documented. In the current study, we performed secondary analyses to investigate the combined effect of AMH and BMI on pregnancy outcomes among women with PCOS who underwent IVF.

Materials and methods**Patients**

The Frefro-PCOS was a randomized trial designed to compare elective frozen embryo transfer with fresh embryo transfer in women with PCOS and was conducted from June 2013 to July 2015 across 14 centers in China (ClinicalTrials.gov; trial number: NCT01841528). The Frefro-PCOS study was approved by the ethics committee of the Center for Reproductive Medicine at Shandong University and all other study sites. Written informed consent was obtained from all participants. The study protocol and main outcomes have been published previously.^{35,36} Briefly, 1508 patients with PCOS who underwent their first cycle of IVF with or without intracytoplasmic sperm administration were enrolled. In the original study, PCOS was diagnosed using the modified Rotterdam criteria, which was the presence of menstrual disturbance combined with either hyperandrogenism (hyperandrogenemia and/or hirsutism) or a polycystic ovary on ultrasonography (defined as either an ovary that contains ≥ 12 antral follicles or an ovarian volume of >10 cm³) after the exclusion of other causes of hyperandrogenism and ovulation dysfunction.³⁵ In addition, patients with abnormal intrauterine cavities, histories of unilateral oophorectomy, histories of recurrent spontaneous abortion, and abnormal parental karyotypes were excluded. All patients were 20 to 35 years of age and weighed ≥ 40 kg.

Here, we included the data of 625 women recruited from the Center for Reproductive Medicine at Shandong University with AMH levels measured before IVF. Patients were grouped by the combinations of percentile range of AMH (25th–75th percentiles) and BMI

(< 24 or ≥ 24 kg/m²).^{37,38} Patients were grouped into 6 groups: group A (normal weight and low AMH group), group B (normal weight and intermediate AMH group), group C (normal weight and high AMH group), group D (overweight/obese and low AMH group), group E (overweight/obese and intermediate AMH group), and group F (overweight/obese and high AMH group).

Serum antimüllerian hormone assay

The serum AMH levels were measured before IVF treatment using enzyme-linked immunosorbent assay (Ansh Labs LLC, Webster, TX).

In vitro fertilization procedures

The detailed procedures of ovarian stimulation, oocyte retrieval, embryo culture, and embryo transfer were performed as previously reported.³⁵ Briefly, ovarian stimulation was achieved using a standard gonadotropin (Gn)-releasing hormone antagonist protocol, during which ultrasound and hormone measurements were used to monitor ovarian responses. When at least 2 leading follicles reached 18 mm, human chorionic gonadotropin (hCG) was administered to induce final oocyte maturation. Patients who were at a low risk of OHSS were randomized to fresh or frozen embryo transfer groups at a 1:1 ratio on the day of oocyte retrieval. On the day of embryo transfer, the risk of OHSS was reevaluated, and fresh embryo transfer was canceled in women who developed OHSS or in those who were at high risk of OHSS. For patients assigned to the fresh embryo transfer group, embryos were transferred on the third day after oocyte retrieval, and intramuscular progesterone was used for luteal phase support. In the frozen embryo transfer group, 2 embryos were vitrified on day 3 of embryo culture. Hormone replacement regimens using oral estradiol valerate and intramuscular progesterone were used for endometrial preparation before frozen embryo transfer. Up to 2 embryos were transferred to each group. If pregnancy was successfully achieved, luteal phase support was continued until 10 weeks of gestation in all patients.

Outcomes

The pregnancy outcomes included the rates of moderate or severe OHSS, live birth, biochemical pregnancy, biochemical miscarriage, clinical pregnancy, clinical miscarriage, preterm delivery, GDM, and preeclampsia. Moderate OHSS was diagnosed on the basis of the presence of abdominal distension; discomfort with/without nausea, vomiting, and/or diarrhea; and ultrasonographic ascites. Severe OHSS was diagnosed when there was clinical evidence of ascites and/or hydrothorax or breathing difficulties with or without hemoconcentration, coagulation abnormalities, or diminished renal function. Live birth was defined as the delivery of any viable neonate after 28 weeks of gestation. Biochemical pregnancy was defined as a serum hCG level of >10 IU/L 14 days after embryo transfer. Biochemical miscarriage was defined as a confirmed biochemical pregnancy that did not progress to a clinical pregnancy. Clinical pregnancy was defined as the presence of at least 1 gestational sac in the uterine cavity on ultrasound 5 weeks after embryo transfer. Clinical miscarriage was defined as a clinical pregnancy that did not progress to a live birth because of a spontaneous or therapeutic ending of clinical pregnancies. Preterm birth was defined as delivery before 37 weeks of gestation. The diagnoses of GDM and preeclampsia were obtained from obstetrical and neonatal medical records.

Statistical analysis

For continuous variables, normality was tested using histograms, Q-Q plots, and the Shapiro-Wilk test. Normally distributed variables are presented as mean \pm standard deviation, whereas nonnormally distributed variables are presented as median (interquartile range). Categorical variables were expressed as the number of cases and the percentage of occurrence. Of note, One-way analysis of variance test or the Kruskal-Wallis test was used to compare continuous data. Categorical variables were assessed using χ^2 analysis or the Fisher exact test, as appropriate. A multivariate logistic regression analysis was performed to evaluate the relationships between treatment and outcomes,

adjusting for confounding factors, including age, AFC, luteinizing hormone (LH), estradiol, total testosterone, and concomitant male factor for infertility. All statistical analyses were performed using the SPSS software (version 26.0; SPSS Inc, Chicago, IL). A *P* value of <.05 was considered to indicate statistical significance.

Results

Baseline characteristics

The baseline characteristics of the patients included in this study are presented in Table 1. Of 625 patients, serum AMH levels were comparable between patients with normal weight (BMI of <24 kg/m²) and those who were overweight/obese (BMI of ≥ 24 kg/m²) in each category of AMH levels. The 25th to 75th percentile ranges of serum AMH levels for patients with normal weight and those who were overweight/obese were 3.59 to 9.82 and 3.46 to 9.37 ng/mL, respectively.

Patients with normal weight and intermediate AMH levels (group B) were younger than those with normal weight and low AMH levels (group A), those with normal weight and high AMH levels (group C), and those who were overweight/obese and had intermediate AMH levels (group E) (*P*=.020, *P*=.001, and *P*=.010, respectively). Patients with the highest AMH levels were associated with the highest AFC, whereas those with the lowest AMH levels had the lowest AFC in both patients with normal weight and those who were overweight/obese. Moreover, for patients with elevated AMH levels, those who were overweight/obese (group F) had a higher AFC (*P*=.003) than those with normal weight (group C). In addition, in patients with normal weight (groups A, B, and C), both high AMH levels (group C) and intermediate AMH levels (group B) were associated with higher baseline serum LH levels (*P*<.001 for group C vs group A and *P*=.001 for group B vs group A) and higher total testosterone levels (*P*<.001 for group C vs group A and *P*=.006 for group B vs group A) than low AMH levels (group A). For patients who were overweight/obese, those with high

TABLE 1
Baseline characteristics of the patients according to AMH and BMI categories

Characteristic	BMI<24 kg/m ²			BMI≥24 kg/m ²			P value
	Group A (normal weight and low AMH group) n=72	Group B (normal weight and intermediate AMH group) n=143	Group C (normal weight and high AMH group) n=72	Group D (overweight/obese and low AMH group) n=85	Group E (overweight/obese and intermediate AMH group) n=168	Group F (overweight/obese and high AMH group) n=85	
AMH range (ng/mL)	0–25th quartile (0.33–3.59)	25th–75th quartile (3.59–9.82)	75th–100th quartile (9.82–18.00)	0–25th quartile (0.58–3.46)	25th–75th quartile (3.46–9.37)	75th–100th quartile (9.37–18.00)	
AMH (ng/mL)	2.31 (1.66–3.14)	5.92 (4.46–8.04) ^a	13.52 (10.71–14.98) ^{b,c}	2.53 (2.02–3.14)	5.62 (4.50–7.47) ^d	12.88 (10.81–14.95) ^{e,f}	<.001
Age (y)	27.00 (25.0–30.75)	26.00 (25.00–29.00) ^{a,g}	28.00 (26.00–30.75) ^c	27.00 (26.00–30.50)	27.50 (26.00–30.00)	28.00 (26.00–31.00)	.004
BMI (kg/m ²)	21.48 (20.34–22.64) ^h	21.23 (20.28–22.66) ^g	21.83 (20.60–22.89) ⁱ	27.18 (25.11–29.38)	26.94 (25.30–29.02)	26.35 (25.11–28.44)	<.001
Primary infertility	28 (38.9%)	37 (25.9%)	22 (30.6%)	26 (30.6%)	60 (35.7%)	22 (25.9%)	.251
AFC	25.00 (23.00–29.00)	28.00 (24.00–33.00) ^a	31.00 (27.00–38.75) ^{b,c,i}	27.00 (22.50–33.0)	30.00 (25.00–36.00) ^d	38.00 (29.00–47.00) ^{e,f}	<.001
Baseline endocrine concentrations							
FSH (IU/L)	5.80 (4.66–7.01)	5.98 (5.12–6.71)	5.74 (5.00–7.06)	5.77 (5.20–6.51)	5.68 (4.92–6.57)	5.40 (4.82–6.18)	.117
LH (IU/L)	6.00 (4.29–10.35)	8.97 (5.69–13.72) ^a	11.08 (6.20–15.62) ^b	7.37 (4.81–11.92)	8.31 (5.19–12.25)	10.60 (7.47–14.84) ^{e,f}	<.001
Estradiol (pg/mL)	33.55 (25.13–46.90)	35.60 (27.10–48.30)	37.85 (29.03–62.20)	33.90 (22.80–43.45)	37.00 (26.40–51.40)	38.30 (31.55–51.30)	.064
Total testosterone (ng/dL)	30.11 (21.97–40.43) ^h	36.74 (27.35–48.35) ^a	42.70 (29.37–53.09) ^{b,i}	35.28 (26.16–48.85)	38.67 (29.78–52.70)	52.57 (36.25–63.78) ^{e,f}	<.001
Concomitant infertility factors							
Tubal factor	47 (65.3%)	97 (67.8%)	47 (65.3%) ⁱ	64 (75.3%)	129 (76.8%)	71 (83.5%)	.029
Male factor	21 (29.2%) ^h	28 (19.6%)	21 (29.2%) ⁱ	9 (10.6%)	27 (16.1%)	4 (4.7%)	<.001

Data are presented as median (interquartile range) or number (percentage), unless otherwise indicated.

AFC, antral follicle count; AMH, antimüllerian hormone; BMI, body mass index; FSH, follicle-stimulating hormone; LH, luteinizing hormone.

^a Significant subgroup difference between the normal weight and low AMH group and normal weight and intermediate AMH group; ^b Significant subgroup difference between the normal weight and low AMH group and normal weight and high AMH group; ^c Significant subgroup difference between the normal weight and intermediate AMH group and normal weight and high AMH group; ^d Significant subgroup difference between overweight/obese and low AMH group and overweight/obese and intermediate AMH group; ^e Significant subgroup difference between overweight/obese and low AMH group and overweight/obese and high AMH group; ^f Significant subgroup difference between overweight/obese and intermediate AMH group and overweight/obese and high AMH group; ^g Significant subgroup difference between the normal weight and intermediate AMH group and overweight/obese and intermediate AMH group; ^h Significant subgroup difference between the normal weight and low AMH group and overweight/obese and low AMH group; ⁱ Significant subgroup difference between normal weight and high AMH group and overweight/obese and high AMH group.

Niu. Combined impact of antimüllerian hormone and body mass index on pregnancy outcomes in women with polycystic ovary syndrome. *Am J Obstet Gynecol Glob Rep* 2025.

AMH levels (group F) also had higher baseline serum LH levels ($P<.001$ for group F vs group D and $P=.001$ for group F vs group E) and higher total testosterone levels ($P<.001$ for group F vs group D and $P<.001$ for group F vs group E) than both those with low AMH levels (group D) and those with intermediate AMH levels (group E). In addition, for both patients with low and high AMH levels, those who were overweight/obese (groups D and F) had higher serum total testosterone levels and lower rates of male factor for infertility than those with normal weight (groups A and C).

Ovarian response

Patients who were overweight/obese were associated with higher starting Gn doses, total Gn doses, and serum LH levels on the day of hCG administration than patients with normal weight in each category of AMH levels (Table 2). Patients with normal weight and low AMH levels (group A) received higher total Gn doses than those with normal weight and high AMH levels (group C) ($P=.041$) and lower estrogen levels on the day of hCG administration than those with normal weight and intermediate AMH levels (group B) ($P=.004$) and those with normal weight and high AMH levels (group C) ($P<.001$). Patients who were overweight/obese and had low AMH levels (group D) had a longer duration of ovarian stimulation ($P=.006$ for group D vs group E and $P=.003$ for group D vs group F) and higher total Gn doses ($P=.019$ for group D vs group E and $P=.001$ for group D vs group F) than those who were overweight/obese and had intermediate AMH levels (group E) and those who were overweight/obese and had high AMH levels (group F). In addition, serum estrogen levels were lower in those who were overweight/obese and had low AMH levels (group D) than in those who were overweight/obese and had high AMH levels (group F) ($P=.003$).

Moreover, patients with normal weight and high AMH levels (group C) yielded a larger number of 14- to 18-mm follicles on the day of hCG administration than both those with normal

weight and low AMH levels (group A) ($P=.012$) and those with normal weight and intermediate AMH levels (group B) ($P=.009$). However, for patients who were overweight/obese, both intermediate (group E) ($P=.042$) and high AMH (group F) levels ($P=.002$) were associated with larger numbers of 14- to 18-mm follicles on the day of hCG administration than low AMH levels (group D). However, there was no difference in the number of oocytes retrieved and the number of good-quality embryos on day 3 among the 6 groups.

Pregnancy outcomes

The pregnancy outcomes are shown in Tables 3. The overweight/obese and high AMH group (group F) had a higher risk of clinical pregnancy miscarriage and OHSS than the overweight/obese and low AMH group (group D) and overweight/obese and intermediate AMH group (group E) (miscarriage: 36.4% in group F vs 18.3% in group D [$P=.023$] and 36.4% in group F vs 18.3% in group E [$P=.012$]; OHSS: 9.4% in group F vs 0.0% in group D [$P=.004$] and 9.4% in group F vs 3.0% in group E [$P=.029$]). In addition, the risk of OHSS was higher in the normal weight and high AMH group (group C) than in the normal weight and intermediate AMH group (group B) (9.7% vs 2.8%, respectively; $P=.030$). We did not find any statistically significant difference in the rates of biochemical pregnancy, clinical pregnancy, and live birth among the 6 groups.

For twin pregnancies, the normal weight and low AMH group (group A) was associated with a higher risk of preterm delivery than the normal weight and intermediate AMH group (group B) and normal weight and high AMH group (group C) (78.6% in group A vs 29.6% in group B [$P=.003$]; 78.6% in group A vs 12.5% in group C [$P=.006$]). In addition, the overweight/obese and intermediate AMH group (group E) had a higher risk of GDM than the normal weight and intermediate AMH group (group B) ($P=.021$).

After adjustment for the confounding factors, including age, AFC, baseline endocrine concentrations (including LH, estradiol, and total testosterone)

and concomitant male factor for infertility in Tables 4, the overweight/obese and high AMH group (group F) was associated with an increased risk of clinical pregnancy miscarriage (adjusted odds ratio [aOR], 3.30; 95% confidence interval [CI], 1.35–8.07) compared with the normal weight and intermediate AMH group (group B). Both the normal weight and high AMH group (group C) (aOR, 3.74; 95% CI, 1.06–13.24) and overweight/obese and high AMH group (group F) (aOR, 3.61; 95% CI, 1.05–12.38) had higher risks of OHSS than the normal weight and intermediate AMH group (group B). Furthermore, the normal weight and low AMH group (group A) was associated with a higher risk of preterm delivery for twin pregnancy (aOR, 12.45; 95% CI, 2.46–63.08) than the normal weight and intermediate AMH group (group B).

Discussion

In women with PCOS, high serum AMH levels accompanied with overweight/obesity significantly increased the risk of clinical pregnancy miscarriage compared with normal weight and intermediate AMH levels. In addition, women with high serum AMH levels were associated with a higher risk of OHSS in both women with normal weight and those who were overweight/obese than those with normal weight and intermediate AMH levels. Furthermore, women with normal weight and low AMH levels had a higher risk of preterm delivery in twin pregnancies than those with normal weight and intermediate AMH levels.

In line with a previous study exploring the correlation between AMH levels and individual features of PCOS,³⁹ our study showed that higher AMH levels were associated with higher AFC, LH, and testosterone levels in both patients with normal weight and those who were overweight/obese. Moreover, the AMH ranges divided by the 25th and 75th percentiles of AMH levels were comparable between patients with normal weight and those who were overweight/obese in our study, which was in accordance with the studies suggesting that

TABLE 2
Ovarian response and embryo transfer

Characteristic	BMI<24 kg/m ²			BMI≥24 kg/m ²			P value
	Group A (normal weight and low AMH group) n=72	Group B (normal weight and intermediate AMH group) n=143	Group C (normal weight and high AMH group) n=72	Group D (overweight/obese and low AMH group) n=85	Group E (overweight/obese and intermediate AMH group) n=168	Group F (overweight/obese and high AMH group) n=85	
Gn starting dose (IU)	112.50 (112.50–140.63) ^a	112.50 (112.50–112.50) ^b	112.50 (112.50–112.50) ^c	150.00 (150.00–150.00)	150.00 (150.00–150.00)	150.00 (150.00–150.00)	<.001
Duration of ovarian stimulation (d)	9.50 (8.25–11.75) ^a	10.00 (9.00–11.00)	9.00 (8.00–11.00)	11.00 (10.00–13.00)	10.00 (9.00–12.00) ^g	10.00 (9.00–11.00) ^h	<.001
Total Gn dose (IU)	1293.75 (1050.00–1743.75) ^a	1200.00 (1033.50–1575.00) ^b	1200.00 (975.00–1462.50) ^{c,e}	2100.00 (1425.00–2756.25)	1725.00 (1321.88–2400.08) ^g	1500.00 (1200.00–2100.00) ^h	<.001
Estrogen level on the day of hCG administration (pg/mL)	3344.50 (2209.25–454375)	4036.00 (2406.00–6674.00) ^d	5248.00 (2935.50–6157.00) ^a	3485.00 (2168.50–5148.50)	4002.00 (2444.00–5852.50)	4689.00 (2892.00–6173.50) ^h	<.001
LH level on the day of hCG administration (IU/L)	1.51 (0.79–3.12) ^a	1.74 (0.81–2.67) ^b	1.65 (0.92–2.76) ^c	2.48 (1.76–4.45)	2.77 (1.37–4.28)	2.56 (1.46–4.55)	<.001
Progesterone level on the day of hCG administration (ng/mL)	0.94 (0.69–1.23)	0.87 (0.62–1.24)	0.87 (0.68–1.23)	0.92 (0.70–1.29)	0.93 (0.71–1.18)	0.90 (0.66–1.29)	.803
Endometrium thickness on the day of hCG administration (mm)	12.00 (10.00–12.50)	11.00 (10.00–12.00)	11.0 (10.00–12.50)	12.00 (10.00–12.50)	11.00 (10.00–12.00)	11.00 (10.00–12.00)	.415
Number of 14–18 mm follicles on the day of hCG administration	6.00 (4.00–8.00)	7.00 (5.00–9.00)	7.00 (6.00–10.00) ^{e,f}	6.00 (4.00–8.00)	7.00 (5.00–9.00) ^g	8.00 (6.00–11.00) ^h	<.001
Number of >18 mm follicles on the day of hCG administration	6.00 (4.00–8.00)	6.00 (4.00–7.00)	7.00 (5.00–8.75)	6.00 (4.00–8.00)	5.00 (4.00–8.00)	6.00 (5.00–8.00)	.126
Number of oocytes retrieved	12.00 (10.00–16.00)	15.00 (1000–18.00)	16.50 (10.00–20.00)	14.00 (10.00–19.00)	15.00 (10.00–18.75)	15.00 (10.00–19.00)	.235
Number of good-quality embryos on day 3	5.00 (3.00–7.00)	5.00 (3.00–8.00)	7.00 (4.00–9.00)	5.00 (2.00–8.00)	5.00 (3.00–8.00)	5.00 (2.00–8.00)	.122
Fertilization methods							<.001
IVF	45 (65.2%) ^a	94 (67.1%)	48 (66.7%) ^c	65 (79.3%)	137 (83.0%) ^g	78 (91.8%)	
ICSI	24 (34.8%)	44 (31.4%)	21 (29.2%)	16 (19.5%)	25 (15.2%)	7 (8.2%)	
IVF + ICSI	0 (0%)	2 (1.4%)	3 (4.2%)	1 (1.2%)	3 (1.8%)	0 (0%)	

Niu. Combined impact of antimüllerian hormone and body mass index on pregnancy outcomes in women with polycystic ovary syndrome. Am J Obstet Gynecol Glob Rep 2025.

(continued)

TABLE 2

Ovarian response and embryo transfer (continued)

Characteristic	BMI<24 kg/m ²			BMI≥24 kg/m ²			P value
	Group A (normal weight and low AMH group) n=72	Group B (normal weight and intermediate AMH group) n=143	Group C (normal weight and high AMH group) n=72	Group D (overweight/obese and low AMH group) n=85	Group E (overweight/obese and intermediate AMH group) n=168	Group F (overweight/obese and high AMH group) n=85	
Number of embryos transferred							.770
1	3 (4.3%)	11 (7.9%)	7 (9.7%)	6 (7.3%)	10 (6.1%)	4 (4.8%)	
2	66 (95.7%)	128 (92.1%)	65 (90.3%)	76 (92.7%)	155 (93.9%)	80 (95.2%)	
Stage of embryo transferred							.589
Cleavage stage	67 (97.1%)	130 (93.05%)	65 (90.3%)	75 (91.5%)	155 (93.9%)	80 (95.2%)	
Blastocyst stage	2 (2.9%)	9 (6.5%)	7 (9.7%)	7 (8.5%)	10 (6.1%)	4 (4.8%)	
Regimen of embryo transfer [†]							.589
Fresh	30 (43.5%)	65 (46.8%)	36 (50.0%)	45 (54.9%)	82 (49.7%)	47 (56.0%)	
Frozen	39 (56.5%)	74 (53.2%)	36 (50.0%)	37 (45.1%)	83 (50.3%)	37 (44.0%)	

AMH, antimüllerian hormone; BMI, body mass index; Gn, gonadotropin; hCG, human chorionic gonadotropin; LH, luteinizing hormone.

Data are presented as median (interquartile range) or number (percentage), unless otherwise indicated.

^a Significant subgroup difference between normal weight and low AMH group and overweight/obese and low AMH group; ^b Significant subgroup difference between normal weight and intermediate AMH group and overweight/obese and intermediate AMH group; ^c Significant subgroup difference between normal weight and high AMH group and overweight/obese and high AMH group; ^d Significant subgroup difference between normal weight and low AMH group and normal weight and intermediate AMH group; ^e Significant subgroup difference between normal weight and low AMH group and normal weight and high AMH group; ^f Significant subgroup difference between normal weight and intermediate AMH group and normal weight and high AMH group; ^g Significant subgroup difference between overweight/obese and low AMH group and overweight/obese and intermediate AMH group; ^h Significant subgroup difference between overweight/obese and low AMH group and overweight/obese and high AMH group; ⁱ Of note, 3 women in the normal weight and low AMH group, 4 women in the normal weight and intermediate AMH group, 3 women in the overweight/obese and low AMH group, 3 women in the overweight/obese and intermediate AMH group, and 1 woman in the overweight/obese and high AMH group did not undergo embryo transfer.

Niu. Combined impact of antimüllerian hormone and body mass index on pregnancy outcomes in women with polycystic ovary syndrome. *Am J Obstet Gynecol Glob Rep* 2025.

TABLE 3
Pregnancy outcomes by different combinations of AMH and BMI categories

Characteristic	BMI < 24 kg/m ²			BMI ≥ 24 kg/m ²			P value
	Group A (normal weight and low AMH group) n=72	Group B (normal weight and intermediate AMH group) n=143	Group C (normal weight and high AMH group) n=72	Group D (overweight/obese and low AMH group) n=85	Group E (overweight/obese and intermediate AMH group) n=168	Group F (overweight/obese and high AMH group) n=85	
Biochemical pregnancy	45/72 (62.5%)	94/143 (65.7%)	47/72 (65.3%)	56/85 (65.9%)	116/168 (69.0%)	58/85 (68.2%)	.943
Biochemical miscarriage	2/45 (4.4%)	9/94 (9.6%)	4/47 (8.5%)	3/56 (5.4%)	10/116 (8.6%)	3/58 (5.2%)	.854
Clinical pregnancy	41/72 (56.9%)	82/143 (57.3%)	43/72 (59.7%)	53/85 (62.4%)	104/168 (61.9%)	55/85 (64.7%)	.865
Singleton	27 (65.9%)	55 (67.1%)	35 (81.4%)	39 (73.6%)	76 (73.1%)	45 (81.8%)	.281
Twin	14 (34.1%)	27 (32.9%)	8 (18.6%)	14 (26.4%)	28 (26.9%)	10 (18.2%)	
Clinical miscarriage	6/41 (14.6%)	10/82 (12.2%)	9/43 (20.9%)	9/53 (18.3%)	19/104 (18.3%)	20/55 (36.4%) ^{e,f}	.017
Live birth ^g	35/72 (48.6%)	71/143 (49.7%)	34/72 (47.2%)	44/85 (51.8%)	85/168 (50.6%)	34/84 (40.5%)	.708
Singleton	21/72 (29.2%)	44/143 (30.8%)	26/72 (36.1%)	30/85 (35.3%)	56/168 (33.3%)	24/84 (28.6%)	.860
Twin	14/72 (19.4%)	27/143 (18.9%)	8/72 (11.1%)	14/85 (16.5%)	29/168 (17.3%)	10/84 (11.9%)	.559
Moderate or severe OHSS	3/72 (4.2%)	4/143 (2.8%)	7/72 (9.7%) ^d	0 (0%)	5/168 (3.0%)	8/85 (9.4%) ^{e,f}	.006
Early OHSS	0 (0%)	3 (2.1%)	4 (5.6%)	0 (0%)	3 (1.8%)	6 (7.1%)	.017
Late OHSS	3 (4.2%)	1 (0.7%)	3 (4.2%)	0 (0%)	2 (1.2%)	2 (2.4%)	.122
Single pregnancies							
Preterm delivery*	0 (0%)	1/55 (1.8%)	1/35 (2.9%)	2/39 (5.1%)	6/76 (7.9%)	4/44 (9.1%)	.390
GDM*	0 (0%)	5/55 (9.1%)	1/35 (2.9%)	3/39 (7.7%)	5/76 (6.6%)	2/44 (4.5%)	.660
Preeclampsia*	0 (0%)	0 (0%)	1/35 (2.9%)	1/39 (2.6%)	1/76 (1.3%)	1/44 (2.3%)	.778
Twin pregnancies							
Preterm delivery	11/14 (78.6%)	8/27 (29.6%) ^b	1/8 (12.5%) ^c	7/14 (50.0%)	13/28 (53.6%)	5/10 (50.0%)	.019
GDM	0 (0%)	0 (0%) ^a	0 (0%)	0 (0%)	5/28 (17.9%)	0 (0%)	.041
Preeclampsia	1/14 (7.1%)	0 (0%)	0 (0%)	0 (0%)	2/28 (7.1%)	2/10 (20.0%)	.142

Data are presented as number/total number (percentage), unless otherwise indicated.

AMH, antimüllerian hormone; BMI, body mass index; OHSS, ovarian hyperstimulation syndrome; GDM, gestational diabetes mellitus.

^a Significant subgroup difference between normal weight and intermediate AMH group and overweight/obese and intermediate AMH group; ^d Significant subgroup difference between normal weight and low AMH group and normal weight and intermediate AMH group;

^c Significant subgroup difference between normal weight and low AMH group and normal weight and high AMH group; ^e Significant subgroup difference between overweight/obese and low AMH group and overweight/obese and high AMH group; ^f Significant subgroup difference between overweight/obese and intermediate AMH group and overweight/obese and high AMH group; ^g Of note, 1 woman with high AMH levels who was overweight/obese was lost to follow-up.

Niu. Combined impact of antimüllerian hormone and body mass index on pregnancy outcomes in women with polycystic ovary syndrome. *Am J Obstet Gynecol Glob Rep* 2025.

TABLE 4
Adjusted odds ratios of pregnancy outcomes by different combinations of AMH and BMI categories

Characteristic	Group A (normal weight and low AMH group) n=72	Group B (normal weight and intermediate AMH group) n=143	Group C (normal weight and high AMH group) n=72	Group D (overweight/obese and low AMH group) n=85	Group E (overweight/obese and intermediate AMH group) n=168	Group F (overweight/obese and high AMH group) n=85
Clinical pregnancy miscarriage	1.31 (0.44–3.90)	1	1.70 (0.63–4.63)	1.48 (0.56–3.93)	1.48 (0.64–3.44)	3.30 (1.35–8.07)
Moderate or severe OHSS	1.51 (0.33–6.94)	1	3.74 (1.06–13.24)	0	1.08 (0.28–4.10)	3.61 (1.05–12.38)
Preterm delivery for twin pregnancies	12.45 (2.46–63.08)	1	0.37 (0.04–3.54)	3.27 (0.78–13.62)	2.84 (0.90–9.02)	2.56 (0.54–12.11)

The covariates in the regression models for the outcomes were age, antral follicle count, luteinizing hormone, estradiol, total testosterone, and concomitant male factors for infertility.
AMH, antimüllerian hormone; OHSS, ovarian hyperstimulation syndrome.
Ntiu. Combined impact of antimüllerian hormone and body mass index on pregnancy outcomes in women with polycystic ovary syndrome. *Am J Obstet Gynecol Glob Rep* 2025.

BMI did not affect the circulating AMH levels in women with PCOS.^{2,24,25} Interestingly, although the 75th to 100th percentile ranges of AMH levels were comparable between patients with normal weight (9.82–18.00 ng/mL) and those who were overweight/obese (9.37–18.00 ng/mL) in our study, women who were overweight/obese and had high AMH levels also had higher AFC than those with normal weight and high AMH levels. This phenomenon may be due to more severe granulosa cell dysfunction in women with PCOS who are overweight/obese and have high serum AMH levels than in those with PCOS with normal weight and high serum AMH levels, which contributes to the down-regulation of AMH secretion by the follicle unit. It has been suggested that women with obesity tend to develop a condition of functional hyperandrogenism.⁴⁰ In the current study, testosterone levels were also higher in women who were overweight/obese and had high AMH levels than in those with normal weight and high AMH levels. The data showed that reproductive and metabolic dysfunctions were more severe in women who were overweight/obese and had high AMH levels than in those with normal weight and high AMH levels, emphasizing the importance of weight management in women with PCOS, especially in those with high serum AMH levels.

Women with PCOS have increased AFC and enhanced granulosa cell activity compared with controls,^{41,42} thereby being at a high risk of OHSS. Serum levels of AMH may represent the number of follicles recruited from the pool of primordial follicles and have been well established as a predictor of OHSS.¹⁷ In line with previous studies,⁴³ our study showed that high AMH levels were associated with a high risk of OHSS and high estrogen levels on the day of hCG administration in women with PCOS. Several studies have investigated the effects of BMI on the risk of OHSS. Low BMI has been suggested to be one of the factors that predispose women to OHSS,^{19,44} whereas obesity was shown to be associated with decreased complication rates in women hospitalized with

OHSS.⁴⁵ However, our data showed that overweight/obesity combined with high AMH levels also contributed to an increased risk of OHSS. These data suggest that, under conditions of high serum AMH levels, the protective effect mediated by obesity-related hemodilution for OHSS may be eliminated. OHSS is associated with adverse outcomes, including pregnancy loss, preterm delivery, and low birthweight.^{46–48} Therefore, extra caution is required in ovarian stimulation in women who are overweight/obese and have high AMH levels.

AMH is characteristically elevated in women with PCOS and is likely to be involved in the pathogenesis of PCOS.⁴⁹ A growing number of studies have explored the correlation between serum AMH levels and IVF outcomes in women with PCOS. A meta-analysis showed that the predictability of AMH for clinical pregnancy in women with PCOS was weaker than that in those with normal or low ovary response.⁵⁰ In addition, Arkfeld et al⁵¹ found that AMH predicts miscarriage in non-PCOS but not in PCOS after fresh embryo transfer. Although AMH is a highly sensitive marker of ovarian reserve,⁵² increased AMH levels have been well established to be associated with PCOS severity,¹³ but it may not accurately reflect the oocyte quality in women with PCOS, thus confounding the association between AMH and IVF outcomes. It has been suggested that women with elevated serum AMH levels have a higher risk of miscarriage than those with normal values in the general population after IVF treatment.^{53,54} However, the effect of high serum AMH levels on miscarriage in women with PCOS remains unknown. The high risk of miscarriage in women with PCOS highlights the need for future research in this area. Previously, we and others have reported that high BMI is one of the risk factors for clinical miscarriage in women with PCOS.^{55–58} In addition to the common hormone disorders in women diagnosed with PCOS, adipose tissue functions as an endocrine organ and causes

dysregulated adipokines in overweight/obesity, which may adversely affect endometrial implantation and other reproductive functions.⁵⁹ In the current study, we conducted a combined analysis of AMH and BMI on the pregnancy outcomes in women with PCOS and found that the risk of clinical miscarriage was significantly elevated in women with PCOS with high serum AMH levels accompanied by overweight/obesity. Our study suggests that BMI-stratified AMH analysis facilitates the identification of high-risk populations for clinical miscarriage in women with PCOS.

Previous studies on PCOS showed that high serum AMH levels were associated with a high risk of preterm delivery in women who achieved single delivery after IVF treatment.^{15,16,38} In addition, we found a tendency of increased risk of preterm delivery for single pregnancies in women with high serum AMH levels, in both women with normal weight and those who were overweight/obese, but without a significant difference, which may be due to the relatively small sample size in our study. Moreover, we observed a significantly increased risk of preterm delivery for twin pregnancies in women with normal weight and low AMH levels compared with those with normal weight and intermediate AMH levels. However, the biological mechanism remains unclear. Our study adds additional evidence to the viewpoint that serum AMH levels are associated with the risk of preterm delivery in women with PCOS and suggests that low serum AMH levels may also increase the risk of preterm delivery, especially in twin pregnancies.

Our study was strengthened by the collection of data from a randomized controlled trial (RCT) using a standard protocol for ovarian stimulation, embryo transfer, and standard tracking of pregnancy outcomes. However, this study has several limitations. First, because of the relatively small sample size, the effect of AMH levels on pregnancy outcomes in women with low BMI was not explored, and subgroup analysis by fresh embryo transfer or frozen embryo transfer was not performed.

Large sample size and multicenter RCTs are needed to further explore the effect of AMH in combination with BMI on pregnancy outcomes. Second, all patients aged 20 to 35 years and used hCG to trigger oocyte maturation, and most patients in our study underwent cleavage-stage embryo transfer. Whether our study could be extrapolated to patients with advanced age, those using a GnRH agonist to trigger oocyte maturation, and those who underwent blastocyst-stage embryo transfer warrants further studies.

Conclusion

We found that high serum AMH levels are associated with a high risk of clinical pregnancy miscarriage in women who are overweight/obese but not in women with normal weight. Women with elevated AMH levels were at a high risk of OHSS, and even when accompanied by a higher BMI, their risk of OHSS was still higher than that in those with normal weight and intermediate AMH levels. In addition, women with normal weight and low AMH levels had a higher risk of preterm delivery in twin pregnancies than those with normal weight and intermediate AMH levels. Further studies are warranted to confirm our findings and explore the underlying mechanisms. ■

CRediT authorship contribution statement

Yue Niu: Writing – original draft, Investigation, Formal analysis, Data curation. **Xinwei Han:** Writing – original draft, Investigation, Formal analysis, Data curation. **Huiying Xiao:** Investigation, Formal analysis, Data curation. **Ruolan Miao:** Investigation, Formal analysis, Data curation. **Gege Ouyang:** Formal analysis, Data curation. **Qian Wang:** Supervision, Conceptualization. **Daimin Wei:** Writing – review & editing, Supervision, Project administration, Funding acquisition, Conceptualization. ■

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