

# Effect of Body Mass Index (BMI) on In Vitro Fertilization (IVF) Outcomes in Women with Polycystic Ovary Syndrome (PCOS)

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## Abstract

**Objective:** Obesity is known to have negative impact on reproductive health and ovarian functions. It may alter endocrine axis and quality of oocytes, and indirectly effect the success of in vitro fertilization (IVF).

**Methods:** Medical records of patients with polycystic ovary syndrome (PCOS) who were applied for IVF between 2018 and 2024 were reviewed. Demographics, indications for reproductive treatment, IVF outcome parameters and the factors contributing to morbidity of treatment were recorded. Student's test with one-way analysis of variance (ANOVA) and Kruskal-Wallis tests were used to compare the variables.  $P < 0.05$  was considered statistically significant.

**Results:** 186 patients with PCOS were divided as lean ( $BMI < 25 \text{ kg/m}^2$ , control), overweight ( $BMI 25\text{--}30 \text{ kg/m}^2$ ) and obese ( $BMI > 30 \text{ kg/m}^2$ ). Mean ages and primary infertility rates were similar (both,  $P > 0.05$ ), but duration of infertility was longer in overweight and obese patients ( $P < 0.05$ ). Although patients with higher BMI required more induction dose for the cycle, number of retrieved oocytes did not change significantly, with achieved chemical and clinical pregnancy (each,  $P > 0.05$ ). Moreover, fertilization rates of transferred oocytes and rates of adverse outcomes during pregnancies were similar in the groups (each,  $P > 0.05$ ). Although overweight and obese patients with PCOS required more gonadotropin induction for IVF cycle (2311 vs 1920 vs 1752 IU, respectively,  $P < 0.05$ ), the numbers of metaphase II and fertilized oocytes were seen to be similar with increasing BMI (each,  $P > 0.05$ ).

**Conclusion:** There is longer infertility duration and a higher requirement for gonadotropins in overweight and obese patients with no effect of BMI on most of IVF parameters such as retrieved oocyte, clinical pregnancy, obstetric complication and delivery rate.

**Keywords:** Body mass index (BMI), polycystic ovary syndrome (PCOS), in vitro fertilization (IVF), pregnancy

## Introduction

A worldwide increase in combined prevalence of overweightness and obesity has been observed in past decades, particularly in women of reproductive age.<sup>1,2</sup> Besides being a risk factor for many chronic disorders such as diabetes mellitus (DM), hypertension (HT), cardiovascular or kidney diseases or certain carcinomas, elevated body mass index (BMI) is reported to be associated with infertility, as well.<sup>3-5</sup> Its negative effects on reproductive health is thought to be primarily via endocrine mechanisms, resulting in decreased number of oocytes. Obesity is also suggested to have detrimental effects on in vitro fertilization (IVF) treatment, by increasing both the amount of gonadotropins used and the cycle cancellation rates.<sup>6</sup> Moreover, there are many studies suggesting its negative impact on pre-term delivery, low birth weight or miscarriage, lower implantation rates, clinical pregnancy, and live birth rates when compared with women of normal weight.<sup>7</sup>

On the other hand, some studies have reported no adverse effects of raised BMIs on IVF outcomes.<sup>8,9</sup> In these studies, except from the higher doses of gonadotropin stimulation, higher risk of IVF cycle cancellations and longer stimulation durations, there are no change in the number of retrieved or mature oocytes, embryo quality, fertilization rates, pregnancy complications or delivery rates. Furthermore, irrespective of the impact on IVF outcomes, some studies have reported no statistically significant differences in dose of gonadotropin stimulation in women with higher BMIs compared with lean or normal weighted women.<sup>10</sup>

In the present study, we aimed to determine whether increasing BMI would adversely affect the results of IVF treatment in infertile women with polycystic ovary syndrome (PCOS).

## Methodology

### Study Design and Data Collection

Patients provided informed written consent to have data from their medical records used in research. The study was approved by our institutions's Ethics' Committee (approval date-no: 28.03.2024-338), and performed in accordance with the relevant guidelines and regulations. Medical records of infertile women with PCOS who were admitted for IVF between January 2018 and January 2024 were reviewed. Demographics, indications for reproductive treatment, IVF parameters with serum anti-Müllerian hormone (AMH) levels, factors contributing to morbidity of treatment and outcomes were recorded. PCOS is defined by the presence of two of three Rotterdam criteria: ovulatory dysfunction, hyperandrogenism and polycystic ovaries on ultrasound, determined by the existence of at least 12 follicles in each ovary between 2 and 9 mm in diameter, or ovarian volume  $> 10 \text{ mL}$ .<sup>11</sup> Further standardization of patients with PCOS was done by selecting cases having serum AMH levels 4 ng/mL or above. BMI is defined as a person's weight in kilograms divided by the square of height in meters. The World Health Organization (WHO) definition of normal or lean ( $BMI < 25 \text{ kg/m}^2$ ), overweight as  $BMI$  of  $25\text{--}30 \text{ kg/m}^2$  and obesity as  $BMI$  of  $> 30 \text{ kg/m}^2$  were included.

### Inclusion and Exclusion Criteria

Patients who are 18 year-old or above and had their baseline estradiol (E2), BMI, and AMH levels recorded during their evaluation were included in the study. Studies on postmenopausal or recently pregnant ( $< 3$  months) women, and women with male infertility factors or chronic inflammatory disorders such as endometriosis, thyroid disease and tubal pathology were

excluded. Women at age >38 were also excluded to prevent mis-conclusion due to expected decrease of AMH in this age group.

### Data Analysis

Statistical package for social sciences (SPSS version 11.5, Chicago, IL, USA) was used for the statistical analysis. Descriptive values were expressed as number (n), percentage (%), median or mean with standard deviation ( $\pm$ SD). Student's t test was used for nominal and categorical values, and Kruskal-Wallis test was used to compare the nonparametric variables. Group comparisons were done with one-way analysis of variance (ANOVA) test to ascertain the group that cause the difference.  $P < 0.05$  was considered statistically significant.

### Ethical Considerations

Medipol University Istanbul Mega Hospital, Ethics' Committee, approval date: 28 March 2024, approval number: 338.

### Results

Of two hundred and eight women with PCOS who were seen to be eligible for our inclusion criteria, 22 patients were

excluded from the study due to cleavage-stage embryo arrest (n = 4), fresh transfer (n = 12) and frozen thaw (n = 6). A total of 186 women with PCOS were included. There was no significant difference in age among normal or lean weight (BMI <25 kg/m<sup>2</sup>, n = 92, 49.4%), overweight (BMI 25–30 kg/m<sup>2</sup>, n = 61, 32.7%) and obesity (BMI >30 kg/m<sup>2</sup>, n = 33, 17.7%) groups (each,  $P > 0.05$ ). The duration of infertility was longer in overweight and obesity groups than in normal weight group (mean  $6.2 \pm 3.6$  vs  $4.2 \pm 2.3$  vs  $3.9 \pm 2.5$  years, respectively,  $P < 0.05$ , Table 1). Increasing BMI was associated with lower random serum AMH levels in infertile women, but this was not statistically significant ( $8.81 \pm 0.6$  vs  $8.11 \pm 0.7$  vs  $7.11 \pm 0.9$  ng/mL, respectively,  $P > 0.05$ , Table 1).

There was no significant difference in estradiol levels (E2) among the groups ( $P > 0.05$ , Table 2). Although overweight and obese patients with PCOS required more gonadotropin induction for IVF cycle (2311 vs 1920 vs 1752 IU, respectively,  $P < 0.05$ , Table 2), the numbers of retrieved, metaphase II and fertilized oocytes were seen to be similar with increasing BMI (each,  $P > 0.05$ , Table 2). Fertilization rates of the transferred oocytes were similar as well. Number of day 3 embryos and frozen embryos on days 4 through 6 were not significantly different. Other parameters such as biochemical and clinical

Table 1. Demographic and descriptive parameters of our infertile patients with polycystic ovary syndrome (PCOS) according to body mass index (BMI) and the change in serum anti-müllerian hormone (AMH)

Parameters	Normal BMI<25 (n = 92)	Overweight BMI 25–30 (n = 61)	Obese BMI>30 (n = 33)	P value
Age (year)	28.72 + 3.5	28.8 + 3.9	29.34 + 3.5	0.705
BMI (kg/m <sup>2</sup> )	21.8 ± 2.1	26.79 ± 1.3	33.55 ± 2.3	<0.05
Duration of infertility (year)	3.9 ± 2.5	4.2 ± 2.3	6.2 ± 3.6	0.041
AMH level at transfer (ng/mL)	8.12 + 5.9	8.82 + 5.5	7.07 + 3.9	0.319

AMH, anti-Müllerian hormone; E2, estradiol; Data are expressed as mean±standard deviation (SD) or number (percent).

Table 2. Effect of BMI on parameters of in vitro fertilization (IVF)

Parameters	Normal BMI<25 (n = 92)	Overweight BMI 25–30 (n = 61)	Obese BMI>30 (n = 33)	P value
Dose of gonadotropin (IU)	1752.8 ± 590	1920 ± 419	2311.87 ± 495	<0.001
Peak E2 (pg/mL)	4602 ± 4072	4638 ± 2875	4455.5 ± 2705	0.677
Number of retrieved oocytes	22.42 ± 10.4	23.78 ± 9.5	21.89 ± 10.7	0.726
Number of metaphase II oocytes	16.26 ± 8.5	17.45 ± 8.1	16.34 ± 8.09	0.752
Number of fertilized oocytes	14.35 ± 7.9	15.02 ± 7.8	14.31 ± 7.2	0.854
Fertilization rate (%)	87.5	86.1	87.7	>0.05
Day 3 embryo	13.8 + 7.8	14.43 ± 7.9	13.69 ± 7.3	0.875
Number of frozen embryos (Day 4, 5, 6)	7.72 + 4.6	8.29 ± 4.3	7.58 ± 3.4	0.658
Biochemical pregnancy rate	53 (57.6%)	39 (63.93%)	17 (51.51%)	0.851
Clinical pregnancy rate	47 (51.08%)	34 (55.73%)	14 (42.42%)	0.679
Miscarriage rate	11 (11.95%)	12 (19.6%)	4 (12.12%)	0.923
Live birth rate	42 (45.65%)	27 (44.26%)	13 (39.39%)	0.711
Preterm birth rate	5 (11.9%)	4 (14.8%)	3 (23.07%)	0.056

IU, international unit; E2, estradiol; n, number; %, percent.

pregnancy rates, miscarriage, live or preterm live births in groups were seen to be changed insignificantly (each,  $P > 0.05$ , Table 2).

## Discussion

In recent decades, increasing evidence in the literature shows that obesity is associated with impaired spontaneous fertility together with adverse pregnancy.<sup>5,6</sup> Therefore, it can also contribute to adverse clinical outcomes following IVF procedures.<sup>7</sup> However, heterogeneity of the available studies in terms of geographic variations, race and population subgroups and outcomes prevents drawing firm conclusions. A previous systemic review and meta-analysis published in 2019 identified a significant negative effect of increased female BMI on IVF results, but numerous studies have been published since then, including large cohort studies from national registries, highlighting the need for an updated review and meta-analysis.<sup>2,12</sup>

In studies of Pinborg et al (2011) and Bailey et al (2014), rate of pregnancy per IVF cycle, number and quality of retrieved oocytes and implantation rates were found to be lower in women with obesity.<sup>13,14</sup> On the other hand, our findings were different since there was no statistically significant difference between groups in oocyte retrieval and implantation rates (both  $p > 0.05$ ). The number of oocytes retrieved was seen to be similar with increasing BMI in parallel to the fertilization rates of the transferred oocytes. However, according to our results, the duration of infertility was found to be longer in overweight and obese patients ( $P < 0.05$ ), and these patients with PCOS required more induction dose for IVF cycles. Therefore, our data is on the contrary to these previous meta-analysis reporting women with increased BMI have worse IVF outcomes than women with a normal BMI, namely, fewer harvested oocytes, fewer available embryos, and lower fertilization rates, and increased number of abortions among women with a BMI  $\geq 30$  kg/m<sup>2</sup>.

In the present study, we also concluded that increasing BMI was associated with lower AMH levels in infertile women with PCOS. However, this was not statistically significant between lean weight, overweight and obese patients ( $P > 0.05$ ). Since aging results in an expected decrease in ovarian reserve, and AMH reflects this physiologic change, we have already excluded women over 38 years and our data suggests that there is not a close association between BMI and AMI.<sup>15,16</sup> On the

other hand, increasing BMI still has adverse effects on duration of infertility and dose of gonadotropins needed. However, there was no effect of BMI on clinical pregnancy, delivery rate and obstetric complications.

The present study has several strengths. It has a comparably large sample size and provides information on treatment practices in such a specific population. This enhances external validity, i.e. the generalisability of the method. On the other hand, main limitations of the study are its retrospective design and observational nature leaving the possibility of confounding bias.

## Conclusion

In conclusion, since worldwide obesity rate continues to rise, clinicians will encounter reproductive-aged women with higher BMIs much more often. There is longer infertility duration and a higher requirement for gonadotropins in obese patients with no effect of BMI on most of IVF parameters such as retrieved oocyte, fertilization rate, biochemical or clinical pregnancy, delivery rate and overall obstetric complications. Increase in BMI in women does not appear to have an adverse effect on IVF outcome. However, preconceptional counselling for obese women can be done as weight reduction helps in reducing infertility period.

## Funding

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## Ethical Approval

Ethics' Committee-approved study.

## Conflict of Interest

There is no conflict of interest that may affect the results of the study.

## Authors' Contribution

The researcher did the conceptualization, methodology, formal analysis, writing, reviewing, editing, investigation, and validation for this study. ■

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