Do BMI or Waıst-to-Hıp Ratıo Interfere wıth The Number of Oocytes Retrıeved ın IVF Cycles?

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Abstract: The effect of obesity on ovarian response to ovulation induction and on *in vitro* fertilization (IVF) outcome is controversial. This controversy might stem from the fact that almost all studies on the subject use body mass index (BMI) for obesity measurement. We aimed to determine which obesity measure predicts the possible effect of obesity on ovarian response in IVF patients. In this retrospective study, patients who presented for IVF and underwent an antagonist protocol were included. Their histories and cycle properties were recorded, as well as their BMI and waist-to-hip (W/H) ratios. A total of 35 patients were included. While normal BMI significantly lowered the gonadotropin dose, normal W/H ratio increased the antral follicle count (AFC). Both BMI and W/H ratio did not significantly affect either the number of oocytes retrieved or the metaphase II oocytes. Ovulation induction during IVF cycles can overcome the adverse effects of obesity on ovarian reserve. Large-sample-sized, well-designed studies must be performed to clarify the best obesity measurement method for infertility treatment and to determine the real effect of obesity on IVF success.

Keywords: Obesity, BMI, Waist/hip ratio, Oocyte retrival, IVF, ICSI.

INTRODUCTION

Obesity is a serious current health problem and its relationship with many diseases is well-established. Many studies have been conducted on the effect of obesity on *in vitro* fertilization (IVF) success and ovarian response.

Bellver *et al*. [1] showed that obesity interferes with embryo quality and cleavage patterns in IVF cycles. A study published in 2012 showed that obesity did not have an adverse effect on embryo quality or pregnancy outcome in women under 38 years of age [2]. Haqhighi *et al*. [3] demonstrated that obesity did not have any effect on IVF success. Only morbid obesity was shown to have an effect on clinical pregnancy outcomes, and IVF success in obese and overweight women was comparable to that of normal weight women [2]. While some studies failed to show a relationship between obesity and IVF outcome [4], other studies could only determine a relationship between obesity and retrieved-oocyte numbers in diminished ovarian reserve patients [5].

On the other hand, a review from Turkey emphasized that obesity interferes with many steps of IVF treatment, including oocyte retrieval [6]. Moragianni *et al*. [7] demonstrated adverse effects of obesity on IVF outcomes in their large-sample-sized retrospective study. In a meta-analysis [8] and in a multi-center study [9], the authors concluded that obesity had unfavorable effects on IVF outcome. Shah *et al*. [10] showed that although obesity did not affect the number of retrieved oocytes, it had some adverse effects on oocyte quality and fertilization.

Literature on the subject has had controversial outcomes. Almost all studies conducted on this subject used body mass index (BMI) as the measure of obesity; however, using only BMI might be the wrong strategy. Interestingly, some studies on the cardiovascular system found protective effects of BMI and as a result a new term, 'obesity paradox,' emerged. Later studies used waist-to-hip (W/H) ratio and wrist circumference (WC) as a measure of obesity, and showed the exact effect of body fat distribution and obesity on the cardiovascular system [11].

We aimed to determine which obesity measure predicts the possible adverse effects of obesity on the number of oocytes retrieved and the cycle outcomes in intracytoplasmic sperm inoculation (ICSI) patients on an antagonist cycle.

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MATERIALSAND METHODS

This retrospective study was conducted at the IVF clinic of Gulhane Military Medical Academy. Ethical committee consent was obtained for the study. Patients who presented to the clinic between April 1 and December 31, 2013, and who underwent an antagonist protocol were included.

Patients with ovarian cysts or endometriomas, who had a history of operations that might affect ovarian reserve, who had polycystic ovarian syndrome (PCOS) according to the Rotterdam criteria, who were older than 40 years of age, and who had chronic disease were excluded.

Sociodemographic properties and histories, including the cycle properties of the participants, were recorded. Early follicular-phase antral follicle count (AFC), 8-hour fasting weight, height, and waist and hip circumferences were measured, and W/H and BMI were calculated as defined in our previous study [12].Overweight was defined as BMI ≥25 kg/m^2 and obese was defined as BMI ≥30 kg/m^2[13].W/H ratio ≤0.85 was defined as normal and >0.85 was defined as high.

A fixed antagonist protocol was started on all patients. Gonadotropin was started on the third day of the menstrual cycle. The starting dose was determined according to the individual's age, BMI, and AFC. According to the ovarian response of the patient, gonadotropin doses were adjusted. On day 5, the antagonist was started in each patient with 0.25 mg of subcutaneous cetrorelix daily until the ovulation trigger day. When at least 2 follicles were >18 mm, ovulation trigger was done with 250 mcgof chorionic gonadotropin alpha. Thirty-six to 38 hours after ovulation trigger, oocyte pick-up (OPU) was performed under general anesthesia. All oocytes were counted and graded by an embryologist, and MI and MII oocytes underwent the ICSI procedure. Total gonadotropin dose used, duration of ovulation induction, and the number and grades of oocytes were recorded.

Statistical analysis was performed with the Statistical Package for Social Sciences version 15.0 (SPSS Inc., Chicago, IL). All continuous variables were expressed as mean ± standard deviation (SD). All measurements were evaluated with the Kolmogorov–Smirnov test and the Shapiro-Wilk test to determine normal distribution. A p-value <0.05 was accepted as a significant result.

RESULTS

A total of 35 patient who met the inclusion criteria were included. Their mean age was 31.48±3.71 years, infertility duration was 4.8±3.51 years, FSH level was 6.73±2.82 IU/L, and BMI was 25.65 kg/m^2.

Participants were divided into two groups according to BMI. There were 23 normal-weight and 12 overweight/obese patients. Sociodemographic and cycle properties of the participants according to their BMI are described in Table **1**.

Participants were also divided into two groups according to their W/H ratio. There were 21 patients in the normal group and 14 patients in the high W/H ratio group. Sociodemographic and cycle properties of the groups are described in Table **2**.

Normal BMI resulted in significantly lower gonadotropin doses and normal W/H ratio resulted in significantly high AFCs. Neither BMI nor W/H ratio significantly affected oocyte numbers.

DISCUSSION AND CONCLUSION

In the current study, we showed that ovulation induction for the IVF cycle can overcome the effects of

Table 1: Socio-Demographic and Cycle Properties of Participants According to BMI

	Normal (BMI≥25kg/m^2)	Obese (BMI<25kg/m^2)	P
Age	31.21	32.00	0.562
FSH (IU/L)	6.99	6.23	0.460
E2 (pg/ml)	64.10	43.40	0.205
LH (IU/L)	6.09	4.95	0.380
AFC	10.68	7.64	0.066
Gonadotropin dose	1912.50	2541.67	0.047
Ovulation induction duration (day)	8.83	9.50	0.281
Number of oocytes	9.22	8.42	0.648
Number of MII oocytes	7.13	5.83	0.451

Table 2: Socio-Demographic and Cycle Properties of Participants According to W/H ratio

	Normal W/H Ratio (≤0.85)	High W/H Ratio (>0.85)	P
Age	30.76	32.57	0.161
FSH (IU/L)	6.65	6.85	0.837
E2 (pg/ml)	47.95	72.04	0.130
LH (IU/L)	5.50	6.03	0.680
AFC	11.16	7.64	0.024
Gonadotropin dose (IU)	1932.73	2421.43	0.115
Ovulation induction duration (day)	8.95	9.21	0.668
Number of oocytes	9.81	7.64	0.197
Number of MII oocytes	7.57	5.36	0.180

obesity on ovarian reserves. Although a high W/H ratio caused lower AFC, the numbers of oocytes retrieved in normal and high W/H ratio groups were not significantly different. While high W/H ratio caused lower AFC, higher BMI did not cause significant changes in AFC. The W/H ratio is a better obesity marker than BMI in predicting AFC. Higher BMI causes higher gonadotropin dose requirements for ovulation induction in IVF cycles.

In a review, not only being obese but also being overweight was shown to be a risk factor for increased gonadotropin doses and decreased pregnancy rates in IVF cycles [14]. In a study that evaluated 220 IVF cycles, patients with W/H≥0.80 had a significantly decreased pregnancy rate [15], but the authors did not mention the number of oocytes retrieved. Moreover, they included PCOS patients in the study. In a large-sample-sized retrospective study, obesity was found to be related to cycle cancellation and ovarian response, but did not interfere with pregnancy rates [16]. Van Swieten [17] also reached similar conclusions. Zhang *et al*. [18] showed that increased BMI resulted in increased gonadotropin doses and induction length, and decreased numbers of retrieved oocytes,but they did not find any effect on pregnancy outcome. Depalo [19] found that obesity resulted in both increased gonadotropin doses and IVF success.

In contrast, some studies failed to show a relationship between obesity and IVF success. Although obesity caused increased gonadotropin doses, intrauterine insemination [20], IVF [21, 22], and ICSI [23] success was not decreased. No relationship was established between BMI and anti-Müllerian hormone [24] or between BMI and AFC [25].

Vilarino *et al*. [26] concluded that BMI was not a good predictor of IVF success, and other measurements for obesity must be studied for this purpose.

Marci *et al*. [22] evaluated 463 patients, and BMI≥25 resulted in increased gonadotropin dose but did not change cycle length or the number of retrieved oocytes. Haghigi *et al*. [3] reviewed 230 first IVF cycles and could not find any relationship between BMI and gonadotropin dose, retrieved oocyte numbers, and mature oocyte numbers. Among PCOS patients, obese and overweight women had significantly decreased numbers of retrieved oocytes and fewer good-quality embryos and implantations [27]. Also, higher gonadotropin doses and increased cycle lengths were required.

The strength of the current study was the exclusion criteria that interfere with ovarian response and the homogeneity of the protocol used for ovulation induction. With those strict selection criteria, many confounding factors were eliminated. The major limitation was the small sample size of the study.

To our knowledge, this is the first study that searches for the best predictive obesity measurement to estimate ovarian response to ovulation induction for IVF.

DISCLOSURE

None.

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