Is BMI Sufficient to Evaluate the Association between Obesity and Ovarian Reserves?

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Abstract: Body fat content and distribution might have an effect on ovarian reserves. Here, we studied the effects of body fat distribution on the antral follicle count (AFC) of women who consulted for infertility. In this two-center study, the ovarian reserves of patients who came to the hospital for infertility treatment was evaluated based on their AFC and early follicular phase follicle-stimulating hormone (FSH) levels. In addition, adiposity was evaluated using their body mass index (BMI) and waist-to-hip ratios (WHRs), the subcutaneous tissue thickness of the bicipital and tricipital regions, and the body adiposity index (BAI). Body fat distribution was evaluated using bioelectrical impedance analysis (BIA). We evaluated 58 patients in this study. While we failed to show a relationship between BMI and WHR based on the AFC, there was a significant relationship between body fat percentage and the AFC. The AFC in patients with < 35% body fat and ≥ 35% body fat was 11.54 ± 4.27 and 9.00 ± 3.95, respectively (p = 0.029). There was no significant relationship between the AFC and the WHR, BAI, and bicipital and tricipital subcutaneous tissue thickness. BMI may not reflect the adiposity of every patient. When evaluating the ovarian reserves of patients, we must consider other measures of obesity that reflect body fatness. Further large studies must be conducted to investigate the relationship between body fat and infertility.

Keywords: Antral follicle count, Body fat distribution, Body mass index, Infertility, Ovary.

INTRODUCTION

Obesity is an increasingly serious health concern worldwide, and its association with many diseases has been demonstrated. Obesity as it relates to infertility is also being studied. The effects of obesity on ovarian reserves are being debated. While some studies reveal negative effects of obesity on ovarian reserves [1-4], others reveal conflicting results [5-6].

All these studies used body mass index (BMI) to determine obesity. Although it is the most commonly used parameter to measure obesity, BMI does not provide an accurate measure of a person's body composition, including body fat [7]. There seems to be an 'obesity paradox', as some studies have shown unexpected beneficial effects of obesity on cardiovascular diseases. Some researchers later showed that WHR and wrist circumference are better predictors of cardiovascular events [8-9]. It was concluded that while some obese people are metabolically healthy, other normal weight people might be metabolically obese [10]. This might be either because of the body fat content or the body fat distribution of individuals.

Adipose tissue can be categorized as truncal adipose tissue, which includes visceral and subcutaneous fat in the thorax and abdomen, and peripheral adipose tissue, which includes subcutaneous fat in the extremities. In a study of menopausal women, it was demonstrated that central adiposity is a stronger cardiac risk factor compared to peripheral adiposity [11].

These conflicting findings result in our hypothesis that the content and distribution of body fat might affect ovarian reserves more than BMI.

Bioelectrical impedance analysis (BIA) is noninvasive, easy, and radiation-free compared to the dual energy X-ray absorptiometry (DEXA) technique used to measure fat distribution in the body. BIA has been demonstrated to be an effective method to estimate total abdominal fat [12]. Previously, it was demonstrated that BIA can be used to accurately estimate body fat distribution, and the results correlate well with DEXA results, except for very obese women (BMI > 35) [13-14].

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In this study, we investigated the possible relationship between ovarian reserves and BMI, WHR, subcutaneous tissue thicknesses measured using calipers, and body fat distribution.

MATERIALS AND METHODS

This two-center study was conducted at Canakkale Onsekiz Mart University (COMU) Hospital and Gulhane Askeri Tip Akademisi (GATA) Hospital between 1 April 2013 and 31 October 2013. Local ethics committee approval and the written consent of the participants were obtained.

Patients with a history of surgery that might affect ovarian reserves and those with ovarian cysts, endometrioma, polycystic ovarian syndrome [15], or chronic illness were excluded, as were patients over 40. After obtaining the consent of patients, their socio-demographic information and medical histories were recorded. A gynecologist examined the patients when they were in the early follicular phase of their menstrual cycle using transvaginal ultrasonography. Their AFC was noted.

The anthropometric measurements of all patients were taken when they were in the early follicular phase of menstruation. The measurements were taken in the morning when the patients were in a fasting state, according to the International Standards for Anthropometric Assessment [16]. Measurements were taken by a dietitian at GATA Hospital and by a well-trained nurse at COMU Hospital. The patients' height, weight, waist and hip circumferences, and foot-to-foot BIA were measured. Next, their BMIs and WHRs were calculated, and their subcutaneous fat thickness in the bicipital and tricipital regions was measured using a skinfold caliper.

Weight to the nearest 0.1 kg was determined using a Tanita multi-frequency body composition analyzer (MC-418MA; Tanita Corporation, Tokyo, Japan). Height to the nearest 0.5 cm was determined using a stadiometer.

BMI was calculated as weight in kilograms divided by height in square meters. According to the World Health Organization (WHO), overweightness is defined as a BMI ≥ 25 kg/m^2, and obesity is defined as a BMI ≥ 30 kg/m^2 [17].

Waist circumference was measured at the level of the umbilicus while patients were standing, and hip circumference was measured at the broadest part of the hip.

WHR was calculated by dividing waist circumference by hip circumference. A WHR ≤ 0.85 was accepted as normal and a WHR > 0.85 was accepted as high.

The BAI was calculated as follows [18]: ((hip circumference)/(height) $^{1.5}$) [18].

BIA was performed using the Tanita multi-frequency body composition analyzer (MC-418MA; Tanita Corporation, Tokyo, Japan). The age, sex, and height of the patients were recorded to the analyzer before measurement. The patients stood on the scale barefooted, holding the analyzer handgrips. Impedance against a small electrical current sent through the body was measured according to the conductive properties of the tissue. Fat mass (FM) has a higher impedance and fat-free mass (FFM) has a lower impedance. The basal metabolic rate, body fat percentage, truncal fat percentage, and fat percentage of the extremities of each patient were automatically calculated by the analyzer.

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

RESULTS

Of the 58 patients included in the study, 15 participated at COMU Hospital and 43 participated at GATA Hospital. The mean age was 32.39 ± 8.76, the duration of infertility was 4.31 ± 2.71 years, the mean follicle-stimulating hormone (FSH) level was 6.59 ± 2.45, the mean luteinizing hormone (LH) level was 5.81 ± 2.26, the mean AFC was 10.21 ± 4.20, and the mean BMI was 25.61± 5.81.

The patients were grouped according to BMI. There were 32 patients in the normal weight group, 14 patients in the overweight group, and 12 patients in the obese group. The AFC and FSH levels of the groups were compared and no significant differences were found (Table **1**).

Next, the patients were grouped according to WHR. There were 38 patients in the normal WHR group and 18 in the high WHR group. There was no significant difference between the groups for either AFC or FSH levels (Table **2**).

Table 1: Comparison of Patients According to BMI

	Normal Weight (n: 35)	Over Weight (n:16)	Obese (n:12)	P
Age	29.69±4.41	30.37±4.01	29.92±4.78	0.873
Duration of infertility	4.08±2.96	5.80±2.68	3.29±1.50	0.042
AFC	11.57±4.05	11.43±5.29	8.83±3.49	0.157
FSH	6.94±2.76	6.45±1.75	5.94±2.02	0.464
LH	5.75±1.98	6.27±3.03	5.30±2.04	0.584
E2	46.67±19.21	50.42±28.38	32.43±13.38	0.161

Table 2: Comparison of AFC According to WHR

	WHR≤0.85 (n: 42)	WHR>0.85 (n: 19)	P
Age	29.38±4.09	30.63±4.81	0.300
Duration of infertility	4.81±3.07	3.53±1.76	0.104
AFC	11.45±4.30	10.05±4.42	0.247
FSH	6.66±1.89	6.71±3.33	0.941
LH	6.11±2.44	5.30±1.96	0.235
E2	46.47±21.95	38.18±18.35	0.161

The patients were then re-grouped according to body fat. There were 37 patients in the normal body fat group and 21 in the high body fat group. The groups were similar in terms of age, infertility duration, and FSH and LH levels; however, the AFC was significantly higher in the normal body fat group compared to the high body fat group (Table **3**).

Table 3: Comparison of AFC According to Body Fat

	Body Fat<35 (n:42)	Body Fat≥35 (n:21)	P
Age	29.62±4.44	30.48±4.13	0.463
Duration of infertility	4.21±2.87	4.62±2.59	0.591
AFC	12.02±4.27	9.00±3.95	0.008
FSH	6.76±2.67	6.38±1.79	0.563
LH	5.89±2.43	5.63±2.03	0.696
E2	46.34±17.67	43.10±29.58	0.633

Next, the patients were further divided into two groups according to AFC. There were 30 patients in the group with an AFC ≤ 10 and 28 in the group with an AFC ≥ 11. When the basal metabolic rates, truncal fat percentage, mean upper extremity and lower extremity fat percentages, BAI, and bicipital and tricipital subcutaneous tissue thickness of these groups were measured, we found no significant differences.

DISCUSSION AND CONCLUSION

While we failed to show a relationship between BMI and AFC, we found that patients with a lower body fat percentage had a significantly higher AFC. AFC is a good ovarian reserve marker to predict the number of retrieved and mature oocytes, which directly affects *in vitro* fertilization (IVF) outcomes [19]. Thus, we used AFC as the predictor of ovarian reserves. The results of studies about obesity and either ovarian reserves or IVF success are conflicting.

Haghighi *et al.* [20] found no relationship between BMI and the number of retrieved oocytes in the first IVF cycle of 230 women. Malhotra *et al.* [1] demonstrated that obesity has no effect on AFC but significantly decreases inhibin B levels. Sahmay *et al.* [2] evaluated 222 premenopausal women and concluded there is no relationship between obesity and ovarian reserves. In a retrospective study conducted in 2010, obesity had no significant adverse effect on early follicular phase FSH levels [3]. Halawaty *et al.* [4] evaluated the ovarian reserves of 50 non-obese and 50 obese premenopausal patients. There was no significant difference between the groups when they compared ovarian reserves. Su *et al.* [6] found significantly decreased anti mullerian hormone (AMH) levels but no relationship between AFC and obesity in the late reproductive period of patients. In a retrospective study of female childhood cancer survivors, it was found that obesity causes lower AMH; however, the patients' AFC was not related to obesity [21]. Spandorfer *et al.* [22] showed that although obese IVF patients have an increased cycle cancellation rate, there are similar pregnancy rates for non-obese IVF patients. Kilic *et al.* [23] also found no relationship between BMI and ovarian response to IVF treatment. Martinuzzi *et al.* [24] also found no relationship between obesity and IVF outcomes in their retrospective study. In a large study of an IVF population, no significant relationship was found between BMI and AFC [25].

Fecundity has been found to be reduced among obese and overweight women [26-28]. In a recent meta-analysis, it was shown that obese and overweight women had worse IVF outcomes compared to normal weight patients [29]. In terms of infertility risk, Esmaeilzadeh *et al.* (30) found a 4.8-fold increment for obese women and a 3.8-fold increment for overweight women. Freeman *et al.* [5] evaluated 122 women in

their late reproductive period and found that women with a BMI ≥ 30 have significantly lower AMH levels compared to patients with a BMI < 30. Hollman *et al.* [31] found that women with a WHR ≥ 0.85 experience more infertility. Zaidi *et al.* [32] showed that increased BMI results in decreased ovarian volume. Ben-Haroush *et al.* [33] found a weak relationship between BMI and AFC. Recently, in a large population-based study of black women, it was found that both increased BMI and central obesity cause reduced fertility and increase the time it takes to get pregnant [34]. Wass *et al.* [35] evaluated 220 women who underwent *in vitro* fertilization embryo transfer (IVF-ET) and grouped patients according to WHR. They concluded that patients with android-type fat distribution had lower pregnancy rates. Buyuk *et al.* [36] found that obese and overweight patients with diminished ovarian reserves have lower serum AMH levels and fewer retrieved oocytes compared to normal weight patients with diminished ovarian reserve Luke *et al.* [37] conducted a study of 152,500 artificial reproductive treatment cycles and concluded that increased BMI increases cycle cancellation rates and pregnancy failure rates.

As concluded in cardiology studies, having a high BMI does not always mean having more adipose tissue. Logically, obesity must affect ovarian reserves due to the metabolic effects of adipocytes. We need to determine the amount of metabolically active adipose tissue rather than the whole body mass of patients when evaluating ovarian reserves.

Our findings are compatible with the literature, which did not find any adverse effects of BMI on AFC. The main limitation of our study is the relatively small sample size, which is due to the strict exclusion criteria. A vast majority of infertile patients who had either polycystic ovaries or endometrioma were excluded from our study. Patients who underwent ovarian surgeries or who were over 40 years old were also excluded.

In conclusion, adiposity rather than obesity has some direct adverse effects on ovarian reserves and might have indirect adverse effects on fertility. To our knowledge, this is the first study that has investigated the effect of body fat on ovarian reserves. The possible effects of body fat and its distribution on infertility and infertility treatment outcomes should be studied further.

DISCLOSURE

None

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