



Does Obesity Impact Assisted Reproductive Outcomes in Patients with Endometriosis?

Endometriozisli Hastalardaki Obezitenin Yardımcı Üreme Tekniklerinin Sonuçları Üzerinde Bir Etkisi var mı?

The Effect of Obesity on Infertile Women with Endometriosis

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Özet

Amaç: Endometriozisli obez ya da aşırı kilolu kadınlardaki in vitro fertilizasyon (İVF) sonuçlarının normal kilodaki endometriozisli kadınlarla aynı olup olmadığı bilinmemektedir. Biz bu çalışmada, endometriozisi olan hastalardaki yardımcı üreme teknikleri üzerine obezitenin etkisini değerlendirmeyi amaçladık. **Gereç ve Yöntem:** Geçirilmiş endometrioma operasyon öyküsü olan ve merkezimizde 2009-2014 yılları arasında İVF-İCSİ tedavisi yapılan 45 kadın bu retrospektif kohort çalışmaya dahil edildi. Hastalar vücut kitle indeksine (VKİ) göre 2 gruba ayrıldı: Grup 1, VKİ ≥ 25 kg/m² olan 15 hastadan, grup 2 ise normal kilodaki (18.5-25 kg/m²) 30 kadından oluşuyordu. İVF-İCSİ karakteristikleri ve sonuçları analiz edildi. Yalnızca taze sikluslar kullanıldı. 38 yaşın üzerindeki hastalar çalışma dışında bırakıldı. VKİ hastaların tıbbi kayıtlarındaki boy ve kilo değerleri yardımıyla hesaplandı. **Bulgular:** Gruplar arasında ortalama yaş, bazal FSH, bazal LH ile ilgili olarak anlamlı bir fark bulamadık. Aşırı kilolu ve obez hastalar normal kilodakilerle karşılaştırıldığında benzer oosit sayısı ($p=0.739$), metafaz 2 oosit sayısı ($p=0.680$), hCG günü pik östradiol düzeyine ($p=0.751$) sahipti. Her iki gruptaki gebelik oranları da benzerdi. **Tartışma:** VKİ, endometrioma operasyonu geçirme öyküsü olan hastalardaki İVF-İCSİ karakteristiklerini ve sonuçlarını etkilemiyor gibi görünmektedir.

Anahtar Kelimeler

Obezite; Vücut Kitle İndeksi; Endometriozis; İVF-İCSİ

Abstract

Aim: It is not known whether overweight or obese women with endometriosis have the same outcomes of in vitro fertilization (IVF) when compared with normal weight patients. In the present study, we aimed to evaluate the impact of obesity on assisted reproductive outcomes in patients with endometriosis. **Material and Method:** A total of 45 women with a history of endometrioma operation who underwent IVF or ICSI treatment from 2009 to 2014 in our center were included in this retrospective cohort study. The patients were divided into two groups according to their body mass index (BMI): Group 1 was composed of 15 patients with a BMI of ≥ 25 kg/m²; group 2 included 30 normal weight women (18.5-25 kg/m²). IVF/ICSI characteristics and outcomes were analyzed. Only fresh cycles were included. Women over the age of 38 were excluded. BMI was calculated by using height and weight information from the medical records. **Results:** There were no significant differences between the groups regarding mean age, basal FSH, and basal LH. The overweight and obese patients had similar numbers of oocytes retrieved ($p=0.739$), metaphase 2 oocytes ($p=0.680$), and peak estradiol levels on HCG administration day ($p=0.751$) compared with the normal weight patients. The clinical pregnancy rate was also similar in the two groups. **Discussion:** BMI does not seem to affect IVF/ICSI characteristics and outcomes in patients with a history of endometrioma operations.

Keywords

Obesity; Body Mass Index; Endometriosis; IVF-ICSI

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Introduction

Obesity has emerged as a prevalent chronic disease recognized as a risk factor for cardiovascular disease and cancer. Bailey et al. [1] investigated the effects of a range of BMIs on in vitro fertilization (IVF) outcomes in polycystic ovary syndrome. Overall, they reported worse outcomes, except for a lower prevalence of ovarian hyperstimulation syndrome, as BMI increased. Earlier animal studies have shown that oocyte development was deteriorated and IVF-ICSI outcome was impaired in patients with high BMI [2, 3]. Obesity may negatively affect the oocyte quality, the endometrial receptivity, or both [4]. Despite considerable advances in assisted reproductive techniques (ART), the influence of obesity on IVF-ICSI outcome remains unclear [5, 6]. Endometriosis is an entity characterized by the presence of endometrial glands and stroma at extrauterine sites. Mechanisms of infertility in women with endometriosis are the overproduction of cytokines and metalloproteinases, ciliary dysfunction, pelvic adhesion, premature ovarian failure, dysfunctional folliculogenesis, and fertilization anomaly [7-12].

Although earlier studies [13, 14] have found no positive association between obesity and endometriosis, Calhaz-Jorge et al. revealed obesity to be one of the most important predictors of endometriosis [15]. Ferrero et al. [16] showed that women with endometriosis had lower body mass index (BMI) and were less frequently obese than control subjects. A higher body mass index was found to decrease the risk of deep, as well as ovarian and pelvic, endometriosis [17].

Indeed, it is not known whether overweight or obese women with endometriosis have the same outcomes of IVF when compared with normal weight patients. In the present study we aimed to evaluate the impact of obesity on assisted reproductive outcomes in patients with endometriosis.

Material and Method

A total of 45 women with a history of endometrioma operation who underwent IVF-ICSI treatment from 2009 to 2014 in our center were included in this retrospective cohort study. The patients were divided into two groups according to their body mass index (BMI): Group 1 was composed of 15 patients with a BMI of ≥ 25 kg/m²; group 2 included 30 normal weight women (18.5-25 kg/m²). Only fresh cycles were included. Women over the age of 38 were excluded. The cases in which testicular sperm extraction (TESE) procedures were performed were not included in the study. BMI was calculated by using height and weight information from the medical records.

Material and Method

A total of 45 women with a history of endometrioma operation who underwent IVF-ICSI treatment from 2009 to 2014 in our center were included in this retrospective cohort study. The patients were divided into two groups according to their body mass index (BMI): Group 1 was composed of 15 patients with a BMI of ≥ 25 kg/m²; group 2 included 30 normal weight women (18.5-25 kg/m²). Only fresh cycles were included. Women over the age of 38 were excluded. The cases in which testicular sperm extraction (TESE) procedures were performed were not included in the study. BMI was calculated by using height and weight information from the medical records.

The study was approved by the ethics' committee and institutional review board of Zekai Tahir Burak Women's Health Research and Education Hospital. Written informed consent was obtained from all volunteers. The pituitary down-regulation was achieved and maintained using the long protocol luteal phase administration of GnRH agonist. The GnRH agonist leuprolide acetate (Lucrin daily; Abbott Cedex, Istanbul, Turkey) was initiated on day 21 of the preceding luteal phase (0.5 mg/d SC) until menses and then the dose was dropped to 0.25 mg/d until triggering ovulation. Recombinant (rec) FSH (Puregon; Organon, Oss, the Netherlands; or Gonal F; Serono, Istanbul, Turkey) was used for ovarian stimulation. The initial gonadotropin dose used for ovarian stimulation was individualized according to the patient's age, baseline serum FSH concentrations on day 3, body mass index, and previous response to ovarian stimulation. The starting regimen was fixed for the first 3 days (100-225 IU rec FSH/ day), and thereafter the dose of gonadotropin was adjusted according to the individual ovarian response. Serum estradiol concentrations and transvaginal ultrasonography were measured routinely every 2-3 days thereafter. Ovulation was triggered by administration of rec HCG (Ovitrelle, 250 µgr, Serono, Istanbul, Turkey) when at least two follicles reached 18 mm diameter. Oocytes were retrieved at 36 hours after HCG injection and subjected to intra-cytoplasmic sperm injection regardless of infertility origin. Gradient method was used for sperm washing. Quinn's sperm washing medium (Sage, Trumbull, CT, USA) was used for sperm preparation. Embryo culturing was performed by using G-MOPS plus, G-IVF plus, G1-plus, G2-plus (Vitro life, Sweden AB, Kungsbacka, Sweden) media.

One or two embryos were transferred on day 3. Rocket Thin wall transfer set (Rocket Medical, Hingham, MA, USA) was utilized for embryo transfer procedure. The luteal phase was supported by using transvaginal progesterone (Crinone 8% vaginal gel® Merck-Serono, Switzerland). Progesterone administration was initiated on the oocyte pick-up day and continued for 12 days (until the serum beta hCG measurement day). In case of pregnancy, progesterone was given until the 12th gestational week. IVF/ICSI characteristics and outcomes were analyzed.

Statistical analysis was performed using SPSS Version 15 (SPSS Inc., Chicago, IL, USA). Chi-squared test was used for categorical variables, and an independent sample t-test was used for continuous variables that were normally distributed. $p < 0.05$ was considered to indicate significance. Results are expressed as mean \pm standard deviation.

Results

A total of 45 women were included in the study. The patient characteristics were homogeneously distributed between the groups. We did not find significant differences between the groups regarding mean age, basal FSH, and basal LH (Table 1). Both groups were also compared according to the number of oocytes retrieved, number of metaphase II oocytes, and clinical pregnancy rate. The overweight and obese patients had a similar number of oocytes retrieved ($p=0.739$), metaphase II oocytes ($p=0.680$), and peak estradiol levels on HCG administration day ($p=0.751$) compared with the normal weight patients. All of these parameters were similar and the differences were not statistically significant. The clinical pregnancy rate was also

similar in the two groups (Table 2).

Table 1. Characteristics of the patients.

	Normal weight 18.5-25 kg/m ²	Overweight-obese >25 kg/m ²	P
Number	30	15	
Age, y	30.8 ± 4.5	28.6 ± 2.8	0.103
BMI (kg/m ²)			
Basal FSH (mIU/mL)	6.9 ± 1.9	6.7 ± 1.6	0.717
Basal LH (mIU/mL)	5.9 ± 2.7	4.7 ± 2.4	0.159
Antral follicle count (%)			0.156
<5	5 (16.7)	2 (13.3)	
>5	25 (83.3)	13 (86.7)	

Table 2. Comparison of the IVF-ICSI outcomes of the patients with endometriosis according to the BMI.

	Normal weight 18.5-25 kg/m ²	Overweight-obese >25 kg/m ²	P
Total FSH dose, IU	2334 ± 1004	2651 ± 1096	0.355
Peak estradiol, pg/mL	1616 ± 1063	1509 ± 674	0.751
Endometrial thickness (mm)	9.5 ± 2.7	9.3 ± 2.5	0.839
Number of oocytes retrieved	8.5 ± 5.0	7.8 ± 4.9	0.739
Number of metaphase II oocytes	6.7 ± 4.4	5.9 ± 3.7	0.680
Clinical pregnancy rate	5 (16.7)	2 (13.3)	0.771

Discussion

In this retrospective cohort study, the association between obesity and IVF-ICSI outcome was studied in patients with endometriosis. Our study has demonstrated that BMI does not seem to affect IVF/ICSI characteristics and outcomes in patients with a history of endometrioma operation. To the best of our knowledge, this is the first study evaluating the impact of obesity on assisted reproductive outcomes in patients with endometriosis. Gesink Law et al. reported that obesity could decrease fecundity and pregnancy rate even in women having regular menstrual cycles [18]. Ramlau-Hansen et al. showed that overweight and obese couples had a higher risk than couples with normal weight of being subfertile [19]. Recent studies demonstrated that weight loss could improve hormonal status and fertility outcome in obese women [20-22]. However, it is difficult to comment on these studies because of the variety of methods used to define obesity and the dissimilarities of outcome measures.

There is conflicting data about endometriosis and its association with infertility. The strength of this association depends on the stage of the endometriosis. There is no reliable study indicating a relationship between early stage endometriosis and infertility [23]. But, it has been shown that severe endometriosis could lead to infertility. In cases of a definitive laparoscopic diagnosis of endometriosis, development of infertility is inevitable [24]. In our study, all the patients underwent endometrioma operation. Hornstein et al. reported poor IVF outcome and low pregnancy rates in women who had undergone prior ovarian surgery due to ovarian endometrioma [25]. A history of previous ovarian surgery is the first limitation of our study, because infertility could have occurred either because of previous ovarian surgery or due to the endometriosis.

Although there is an inverse relationship between obesity and endometriosis, it remains unclear. Hediger et al. found that endometriosis tends to occur in patients with lower body mass index [26]. They investigated total 84 women [32 with endometriosis and 52 healthy controls]. The study group was found to be significantly taller, thinner, and with a lower BMI than the control group. Lafay Pillet et al. reported that deep infiltrating endometriosis was more common in thinner women than normal weight ones [27]. The primary goal of our study was to assess the effect of obesity on assisted reproductive outcome in patients with endometriosis. Therefore, the association between obesity and endometriosis was not analyzed.

In conclusion, we did not find any significant differences between the two groups regarding number of oocytes retrieved, metaphase 2 oocytes, or peak estradiol levels on HCG administration day. Also, clinical pregnancy rate was similar in both groups. Our results demonstrate that BMI might not have an impact on ART cycles in patients with a history of endometrioma operation. However, large prospective randomized controlled studies are required to evaluate the impact of obesity on assisted reproductive outcomes in patients with endometriosis.

Competing interests

The authors declare that they have no competing interests.

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