

The relationship between embryo quality and obesity in IVF patients: a single-center retrospective study

IVF hastalarında embriyo kalitesi ve obezite arasındaki ilişki: tek merkezli retrospektif bir çalışma

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Abstract

Purpose: The aim of this study is to retrospectively compare the relationship between female obesity and embryo quality and pregnancy outcome.

Materials and methods: In this retrospective study, which received approval by the ethical committee, data of in vitro fertilization (IVF) patients (n:542) between January 2019 and August 2021 were examined. The patients were divided into four groups: Group 1, Body Mass Index (BMI) <18.50 kg/m² (n:16); Group 2, BMI 18.50-24.99 kg/m² (n:263); Group 3, BMI 25.00-29.99 kg/m² (n:156); Group 4, BMI ≥30 kg/m² (n:107). Demographic characteristics of patients, baseline hormone levels, treatment protocols employed, counts of collected oocytes, day of embryo transfer, transferred embryo quality, a positive pregnancy test, and live births were collected, and statistical analysis was performed.

Results: There were no significant differences between the groups in terms of age, collected oocyte count, number of mature oocytes, maturation rate ($p>0.05$). Group 4 showed a statistically significant decrease in the number of 2PN ($p=0.014$) and fertilised oocyte count ($p=0.006$) compared to Group 2. When comparing pregnancy outcomes based on BMI groups, it was found that obesity did not significantly affect positive/negative pregnancy rates, live birth rates, miscarriage rates, biochemical pregnancy rates among the groups ($p>0.05$). Logistic regression analysis indicated a decrease in embryo quality with increasing age. Multiple regression analysis (MRA) results showed that a good quality of the transferred embryo had a positive impact on achieving a positive pregnancy outcome. The presence of pregnancy was negatively affected by increasing age. In Group 1 and Group 2, there were significantly more Day-5 transfers than in Group 4 ($p=0.008$).

Conclusion: This study showed that obese patients had a lower rate of Day 5 embryos compared to non-obese patients. However, no difference was found between BMI and pregnancy rates. The development of good quality embryos had a favourable effect on pregnancy outcomes, whereas increasing age had a negative effect. The present data suggest that further studies evaluating the mechanism underlying the effect of obesity on embryo development are warranted.

Keywords: Assisted reproduction, infertility, oocyte, body mass index, embryo quality.

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Öz

Amaç: Bu çalışmanın amacı, kadın obezitesi ile embriyo kalitesi ve gebelik sonuçları arasındaki ilişkiyi retrospektif olarak karşılaştırmaktır.

Gereç ve yöntem: Etik kurul onayı alan bu retrospektif çalışmada, Ocak 2019-Ağustos 2021 tarihleri arasında in vitro fertilizasyon (IVF) hastalarının (n:542) verileri incelendi. Hastalar dört gruba ayrılmıştır: Grup 1, Vücut Kitle İndeksi (VKİ) <18,50 kg/m² (n:16); Grup 2, VKİ 18,50-24,99 kg/m² (n:263); Grup 3, VKİ 25,00-29,99 kg/m² (n:156); Grup 4, VKİ ≥30 kg/m² (n:107). Hastaların demografik özellikleri, başlangıç hormon düzeyleri, uygulanan tedavi protokolleri, toplanan oosit sayıları, embriyo transfer günü, transfer edilen embriyo kalitesi, pozitif gebelik testi ve canlı doğumlar toplanmış ve istatistiksel analiz yapılmıştır.

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Bulgular: Gruplar arasında yaş, toplanan oosit sayısı, olgun oosit sayısı ve olgunlaşma oranı açısından anlamlı bir fark yoktu ($p>0,05$). Grup 4'de Grup 2'ye göre 2 PN sayısı ($p=0,014$) ve fertilize olan oosit sayısı ($p=0,006$) istatistiksel olarak anlamlı azalmıştı. VKİ gruplarına göre gebelik sonuçları karşılaştırıldığında, obezitenin gruplar arasında pozitif/negatif gebelik oranlarını, canlı doğum oranlarını, düşük oranlarını ve biyokimyasal gebelik oranlarını önemli ölçüde etkilemediği bulunmuştur ($p>0,05$). Lojistik regresyon analizi, artan yaşla birlikte embriyo kalitesinde azalma olduğunu göstermiştir. Çoklu regresyon analizi (MRA) sonuçları, transfer edilen embriyo kalitesinin iyi olmasının olumlu gebelik sonucu elde edilmesini olumlu yönde etkilediğini göstermiştir. Gebelik varlığı artan yaştan olumsuz etkilenmiştir. Grup 1 ve Grup 2'de, Grup 4'e kıyasla anlamlı derecede daha fazla 5. Gün transferi yapılmıştır ($p=0,008$).

Sonuç: Bu çalışma obez hastaların obez olmayan hastalara kıyasla daha düşük 5. Gün embriyo oranına sahip olduğunu göstermiştir. Bununla birlikte, VKİ ile gebelik oranları arasında fark bulunmamıştır. İyi kalitede embriyo gelişimi gebelik sonuçları üzerinde olumlu bir etkiye sahipken, artan yaş olumsuz bir etkiye sahiptir. Mevcut veriler, obezitenin embriyo gelişimi üzerindeki etkisinin altında yatan mekanizmayı değerlendiren daha ileri çalışmalara ihtiyaç olduğunu göstermektedir.

Anahtar kelimeler: Yardımla üreme, infertilite, oosit, vücut kitle indeksi, embriyo kalitesi.

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Introduction

Obesity and being overweight affect almost every aspect of a woman's reproductive life, from puberty to pregnancy. The risk of anovulation, menstrual disorders, and infertility is increased in obese women. Obesity has a negative effect on pregnancy outcomes [1-3]. Obesity leads to impaired fertility associated with anovulation. The obese infertile female population has been associated with worse in vitro fertilization (IVF) results, using higher doses of gonadotropins, increased cycle cancellation/failure rate, reduced oocyte recovery, and increased miscarriage rate [4].

Obese women showed a significant negative correlation between obesity and live birth after IVF compared with normal-weight women [4]. The changing hypothalamic-pituitary axis function in association with high levels of androgens, estrogen, and insulin may be involved in the disruption of ovarian folliculogenesis [5]. Another retrospective cohort study found no statistically significant difference in implantation rates between obese and non-obese patients. It was found that implantation rate, live birth rate, and risk of miscarriage were not associated with obesity. Nevertheless, it was determined that this may result in a reduction in the implantation rate, given that it renders transfers more challenging for women with a higher Body Mass Index (BMI) [6].

There is no definitive information on the impact of the BMI on the quality of the embryo. However, although the available research data

is partially inconsistent, a study found that slower embryo development was associated with maternal overweight and obesity [7]. The primary objective of the present study was the retrospective analysis of the impact of obesity on fertilisation rates, embryo quality, and live birth rates in patients undergoing IVF treatment at the Pamukkale University IVF Centre between January 2019 and August 2021. The study also aimed to evaluate whether obesity had any effect on the demographic characteristics of these patients.

Materials and methods

Study population

In the retrospective study, which was approved by the Pamukkale University Non-Interventional Clinical Research Ethics Committee (approval date: 31/08/2021; approval number: 16), data of IVF patients who sought treatment at the Pamukkale University IVF Center between January 2019 and August 2021 were examined. Only the data from the first fresh IVF cycle of the patients included in the study were analyzed. Frozen embryo cycles or second cycles of the patients were not included. Patient characteristics, BMI, and laboratory variables were collected from IVF center files.

The exclusion criteria were determined as those with maternal age >42 , patients without embryo transfer, patients with FET cycles, patients undergoing chemotherapy or radiation exposure in their history, and patients with an azoospermic partner.

Body mass measurements were taken on the second day of the menstrual cycle using the calibrated scales available at the IVF center. Group classification was based on data retrieved from patient records. The BMI of an individual is calculated by dividing their weight in kilograms by the square of their height in metres (kg/m²). According to the World Health Organisation (WHO), categorical BMI classification is as follows: Group 1, BMI <18.50 kg/m² (n:16); Group 2, BMI 18.50-24.99 kg/m² (n:263); Group 3, BMI 25.00-29.99 kg/m² (n:156); Group 4, BMI ≥30 kg/m² (n:107) [8].

After the patients were grouped, information was collected about demographic characteristics, hormone levels, treatment protocols used, collected oocyte counts, maturity rate, fertilization rate, embryo transfer day, embryo quality, pregnancy development, and live births.

Ovarian stimulation

Patients were subjected to controlled ovarian hyperstimulation (COH) using the flexible protocol for gonadotropin-releasing hormone (GnRH) antagonists. On the 2nd day of menstruation, the patient was assessed through transvaginal ultrasonography, and basal levels of Follicle-stimulating hormone (FSH), Luteinizing hormone (LH), and Estradiol (E2) were measured. Ovulation induction then began with gonadotropins. When the follicle size reached 14 mm, 250 µg of GnRH antagonist was started daily. The patient's follicle was monitored through ultrasonography. When at least two follicles had reached a size of 18 mm, recombinant Human chorionic gonadotropin (hCG) was administered for oocyte maturation, followed by oocyte pick-up (OPU) after 36 hours.

Laboratory procedure

The collected cumulus-oocyte complexes were placed in a culture medium (GTL, Vitrolife Co., Switzerland) in an incubator at 37°C with 5% O₂ and 6% CO₂. Each oocyte was denuded using the hyaluronidase (Vitrolife Co., Switzerland) enzyme and then mechanically during follow-up. Only patients who underwent ICSI were included in our study. ICSI was

performed on mature oocytes. Fertilization was checked 16-20 hours post-ICSI. Embryonic development was assessed by morphological grading [9, 10]. Embryo quality was evaluated on days 1, 2, and 3 based on blastomere number, blastomere shape, and fragmentation. On day 3, Grade 1 and Grade 2 embryos were considered to be of good quality. On day 5, the number of trophectoderm cells, internal cell mass, and width of the blastocoel cavity were assessed. Embryos with a grade of 3AA, 4AA, or hatching were considered to have good quality. The transfer day was determined according to the embryos quality. A hCG measurement was performed for the patient on Day-11 post-transfer. The presence of one or more gestational sacs on transvaginal ultrasonography was defined as a clinical pregnancy. A biochemical pregnancy (BP) was characterized by a plasma β-hCG concentration exceeding 13 mIU/mL, while miscarriage was defined as pregnancy loss occurring before 20 weeks of gestation. Patients who delivered a viable infant were classified as having achieved a live birth. In all study groups, luteal support for patients who achieved pregnancy was continued until Week-10 of gestation.

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Statistical analysis

All statistical analyses were performed using SPSS 25.0 (IBM SPSS Statistics 25 software (Armonk, NY: IBM Corp.)). Continuous variables were defined by the mean ± standard deviation, and median (IQR: 25th and 75th percentiles). The Kolmogorov-Smirnov and Shapiro-Wilk tests were used for the determination of normal distribution. For independent group comparisons, Kruskal Wallis Variance Analysis (post hoc: Mann-Whitney U test with Bonferroni Correction) was used when parametric test assumptions were not provided. The chi-Square test was used for categorical variables. Logistic regression analysis was used for determining the risk factors for pregnancy. Statistical significance was determined at $p \leq 0.05$.

Results

A total of 542 fresh IVF cycles were examined. Group 1, Group 2, Group 3, and Group 4 had an average BMI of 17.64, 22.18, 27.18, and 33.45, respectively. The average age was similar among the groups (30.06, 32.17, 32.78, and 32.85, respectively). No significant difference was found among the groups in terms of maternal age, number of oocytes collected, number of M2 oocytes, rate of maturation, rate the rate of fertilization, rate of 2PN formation, and number of oocytes fertilized ($p>0.05$). The number of 2PN formation was significantly

higher in Group 2 than in Group 4 ($p=0.014$). The rate of fertilization was significantly higher in Group 1 and Group 2 than in Group 4 ($p=0.006$). When we compared blood hormone levels, there was no significant difference between baseline E2, AMH, and OPU-day E2 levels. Basal serum FSH level was significantly higher in Group 1 and Group 2 than in Group 3 and Group 4 ($p=0.0001$) Basal LH levels were significantly lower in Group 4 than in the other groups ($p=0.0001$). The progesterone level on the hCG day was significantly higher in Group 2 than in Group 3 and Group 4 ($p=0.001$) (Tables 1, 2).

Table 1. Demographic characteristics by BMI groups

	Group 1 (n=16) mean±SD median (Q1-Q3)	Group 2 (n=263) mean±SD median (Q1-Q3)	Group 2 (n=156) mean±SD median (Q1-Q3)	Group 4 (n=107) mean±SD median (Q1-Q3)	p value
Female Age (years)	30.06±5.07 30 (26.25-32.75)	32.17±4.65 32 (29.36-36.75)	32.78±4.95 33 (29.00-36.75)	32.85±5.18 33 (29.00-37.00)	0.1190 (kw=5.856)
Basal FSH (IU/L)	8.05±2.76 7.5 (6.16-9.09)*	8.92±4.73 7.87 (6.36-10.23)*	7.46±2.93 6.78 (5.59-9.07)	7.04±2.62 6.6 (5.45-8.41)	0.0001* (kw=26.186)
Basal LH (IU/L)	7.89±2.82 7.83 (4.97-10.29)	7.06±2.92 6.52 (5.36-8.38)	6.2±3.53 5.43 (4.19-7.14)	5.92±4.82 4.75 (3.68-6.58)**	0.0001** (kw=42.643)
Basal E2 (ng/L)	41.51±16.27 39.75 (26.01-58.15)	44.62±31.33 40.8 (29.22-53.28)	42.56±33.88 36.2 (27.4-46.06)	39.75±24.65 33.44 (25.87-51.06)	0.082 (kw=6.716)
AMH (ng/mL)	2.87±2.31 1.9 (1.2-4.06)	2.16±2.09 1.58 (0.61-3.13)	2.19±1.78 1.78 (0.83-3.1)	2.41±1.79 1.99 (0.91-3.6)	0.289 (kw=3.756)
E2 level on OPU day (ng/L)	1303.75±672.77 1050 (795-1898)	998.71±681.35 844.5 (502.25-1355.5)	1079.84±649.22 983 (532-1632)	1028.85±733.96 (447.25-1383.5)	0.296 (kw=3.698)
Progesterone level on hCG day (µg/mL)	0.67±0.59 0.56 (0.31-0.84)	0.69±0.55 0.57 (0.37-0.85)*	0.59±0.6 0.48 (0.31-0.69)	0.50±0.49 0.34 (0.21-0.61)	0.0001* (kw=29.387)

Group 1, BMI <18.50 kg/m² (n:16); Group 2, BMI 18.50-24.99 kg/m² (n:263); Group 3, BMI 25.00-29.99 kg/m² (n:156)
Group 4, BMI ≥30 kg/m² (n:107) BMI: Body mass index, FSH: follicle-stimulating hormone; hCG: human chorionic gonadotropin
AMH: Anti-mullerian hormone, E2: Estradiol, LH: Luteinizing hormone, The values are presented as the mean (±SD)
IQR: Interquartile range, MII: Metaphase II. kw: Kruskal-Wallis test, * $p<0.05$, in comparison with the Group 3 and Group 4
** $p<0.05$, in comparison with the other groups

Table 2. Cycle characteristics by BMI groups

	Group 1 (n=16) mean±SD median (Q1-Q3)	Group 2 (n=263) mean±SD median (Q1-Q3)	Group 3 (n=156) mean±SD median (Q1-Q3)	Group 4 (n=107) mean±SD median (Q1-Q3)	p value
Number of retrieved oocyte	13.13±6.82 11.5 (7.25-19)	10.56±7.17 10 (5-14)	10.72±7.02 9 (5-16)	9.23±6.14 8 (5-13)	0.102 (kw=6.204)
M2 oocytes (Mean ±SD)	10.88±6.85 10 (5.25-16.25)	8.75±6.12 8 (4-12)	8.68±5.52 8 (4-13)	7.32±5.43 6 (4-10)	0.056 (kw=7.557)
Maturity rate (%)	77.94±21.59 86.61 (71.99-90.6)	84±18.82 89.29 (75-100)	82.57±18.52 87.5 (71.57- 100)	79.56±21.86 85 (66.67-100)	0.173 (kw=4.979)
Fertilization rate (%)	79.86±15.14 78.46 (67.86-97.37)	74.42±19.92 75 (62.5-89.04)	72.35±20.93 75 (60-88.89)	71.39±21.19 75 (57.14-87.5)	0.298 (kw=3.678)
Number of 2PN	7.63±5.04 7 (3.25-10.75)	5.92±4.43 5 (2-8)*	5.61±3.93 4 (2.25-8)	4.49±3.34 3 (2-6)	0.014* (kw=10.662)
Number of fertilized oocytes	8.75±5.3 8.5 (1-20)*	6.4±4.71 5 (1-25)*	6.1±4.27 5 (1-18)	4.95±3.75 4 (1-18)	0.006* (kw=12.362)
Good quality embryos (n-%)	14 (87.50)	191 (72.60)	105 (67.30)	72 (70.50)	0.503 (cs=5.320)
Number of embryos per transfer	1.56±0.51 2 (1-2)	1.57±0.50 2 (1-2)	1.69±0.46 2 (1-2)	1.58±0.50 2 (1-2)	0.206 (kw=4.568)
Day of embryo transfer					
Day3	3 (18.80)	106 (40.30)	69 (44.20)	59 (55.10)	0.012* (cs=10.989)
Day5	13 (81.20)*	157 (59.70)*	87 (55.80)	48 (44.90)	
Endometrial thickness	11.41±2.91 11.05 (10.05-11.97)	11.09±2.39 10.8 (9.4-12.5)	11.6±2.44 11.4 (9.82-13.08)	11.19±2.44 11 (9.6-12.7)	0.205 (kw=4.578)

Group 1, BMI <18.50 kg/m² (n:16); Group 2, BMI 18.50-24.99 kg/m² (n:263); Group 3, BMI 25.00-29.99 kg/m² (n:156); Group 4, BMI ≥30 kg/m² (n:107) BMI: Body mass index, The values are presented as the mean (±SD), IQR: Interquartile range
MII: Metaphase II. PN: Pronucleus. kw: Kruskal–Wallis test, cs: Chi square, * p<0.05, in comparison with the Group 4

The logistic regression analysis revealed a significant difference between age and embryo quality. As age increased, the quality of the embryo decreased. The results of multiple regression analyses showed that good embryo quality had a positive effect on a positive pregnancy test. It was found that a positive pregnancy test was negatively affected by the increase in age. However, no significant difference was found in multiple regression analysis results based on BMI.

The paired comparisons using the Bonferroni correction showed significant differences between transfer days (p=0.008). In Group 1 and Group 2, there were significantly more Day-5 transfers than in Group 4. According to this finding, it was determined that the number of embryos on Day-5 was lower in obese patients (Table 2).

When comparing pregnancy outcomes based on BMI, it was found that obesity did not significantly affect positive/negative pregnancy

rates, live birth rates, miscarriage rates, or biochemical pregnancy rates among the groups ($p>0.05$) (Table 3).

Table 3. Pregnancy outcomes by BMI groups

	Group 1 (n=16) %	Group 2 (n=263) %	Group 3 (n=15) %	Group 4 (n=107) %	p value
Pregnancy positive	10 (62.50)	115 (43.75)	68 (43.60)	56 (52.30)	0.22 (cs=4.395)
Pregnancy negative	6 (37.50)	148 (56.25)	88 (56.40)	51 (47.70)	
Course of pregnancy					
Live birth	8 (80)	79 (68.70)	49 (72.05)	44 (78.58)	0.408 (cs=9.324)
Biochemical	0 (0)	17 (14.79)	8 (11.77)	3 (5.36)	
Miscarriage (1st trimester)	1 (10)	16 (13.91)	8 (11.77)	5 (8.92)	
Miscarriage (2nd trimester)	1 (10)	3 (2.60)	3 (4.41)	4 (7.14)	

Group 1, BMI <18.50 kg/m² (n:16);

Group 2, BMI 18.50-24.99 kg/m² (n:263); Group 3, BMI 25.00-29.99 kg/m² (n:156)

Group 4, BMI ≥30 kg/m² (n:107) BMI: Body mass index. cs: Chi square, * $p<0.05$

Discussion

This study evaluated the impacts of female BMI on embryo development, positive pregnancy rates, live birth rates, and miscarriage rates. With our retrospective examination, we have reported once again how age and good-quality embryo transfer have an impact on pregnancy positivity. The day 5 embryo transfer rate was significantly higher in Group 1 and Group 2 compared to obese patients' rates. The changing function of the hypothalamic-pituitary axis associated with high levels of insulin, androgen, and estrogen may be involved in the disruption of folliculogenesis [5]. Obesity, especially abdominal phenotype, is associated with increased synthesis and storage in fat tissue and a parallel increase in estrone, E2, and testosterone, dihydrotestosterone, androstenedione, and dehydroepiandrosterone. High ovarian androgen levels contribute to anovulation, causing early follicular atresia. Hyper-estrogenism can have a detrimental effect on endometrial receptivity and therefore contribute to infertility [11]. In our study, there was no significant difference between groups in basal E2, AMH, and OPU-day E2 levels.

A study on high-fat diet- and gene mutation-induced (ob/ob) obesity in mice revealed that obesity disrupts oocyte maturation and polarity, impairs spindle morphology, and causes abnormal mitochondrial distribution with early

apoptotic signals, likely through oxidative stress-induced mitochondrial dysfunction [12]. Embryos with massive aneuploidy are likely to result from these defects, thus causing spontaneous abortions. Similar results were obtained in human studies in which unsuccessfully fertilized oocytes were compared from patients, indicating that the prevalence of "disarrayed meiotic spindles with non-aligned chromosomes" in women with obesity was significantly higher [13]. Studies on mice with diet-induced obesity have shown that endometrial decidualization is impaired [14]. A retrospective study in the Italian population examined 1.602 women who underwent the first IVF cycle. Compared with obese and normal-weight patients, there was a significant decrease in the percentage of mature oocytes in obese patients [15]. In contrast to these studies, there were no significant differences between BMI categories for other IVF-ICSI cycle results measured in another study, including the number of oocytes picked-up, mature oocytes, embryos for transfer, the proportion of fertilized oocytes, and cycle cancellation rates ($p>0.05$) [16]. In the present study, there were no significant differences between the groups in terms of collected oocyte count, number of M2 oocytes, maturation rate, fertilization rate ($p>0.05$). But the number of 2PN formation was significantly higher in Group 2 than in Group 4 ($p=0.014$). The number of fertilization was

significantly higher in Group 1 and Group 2 than in Group 4 ($p=0.006$).

A study involving 6,500 IVF cycles reported reduced implantation, pregnancy, and live birth rates in obese women, but no significant difference in oocyte or embryo quality was observed [17]. Using a time-lapse incubator, Fawarseh et al. [18] studied the effect of maternal BMI on embryo morphokinetics. It was found that oocytes from obese patients had slower formation of the second polar body (tPB2) after fertilisation and that the two pronuclear phases were later than in normal-weight women. The t3 and t5-t8 cleavage phases were significantly faster in oocytes retrieved from underweight and overweight women compared to normal BMI. Although it was not statistically significant that cycle outcomes were better in the normal weight group, embryos from normal weight patients had slower cleavage rates than those from obese patients, which is consistent with previous studies where embryo quality was similar. The researchers have argued that the selection of embryos that divide at a slower rate may be associated with better embryo quality [18]. Another study evaluating maternal BMI and embryo morphokinetics found that after the results were corrected for maternal and paternal age and infertility, the time to reach 5 blastomeres (t5) and 8 blastomeres (t8) was longer for obese women than for normal BMI women [7]. In the 6,569 first fresh IVF-ET cycles, which evaluated the impact of both male and female obesity on IVF outcomes, it was found that compared with the normal-BMI group, there were a much lower number of high-quality and usable embryos in the female overweight/obesity and combined male/female overweight/obesity groups ($p<0.05$) [19]. In another study, 617 GnRH antagonist cycles and 1,784 live embryos, no substantial disparities were observed among the various BMI categories with respect to the number of oocytes retrieved, oocyte maturation rate, fertilisation rate, number of embryos created, embryo discard rate, and pregnancy rates. No significant differences were observed between BMI groups in any of the embryo morphokinetic parameters. The study found that maternal body weight, including in the high BMI subgroups, did not have an impact on morphokinetic parameters and embryo quality [20]. In our study, there was no significant difference between embryo quality and BMI. In

line with previous studies, our findings indicate a statistically significant decrease in the rate of fifth-day embryo transfers among obese patients. This reduced rate may be attributed to the lower cleavage rate observed in obese individuals, a factor that has been similarly reported in studies analyzing embryo morphokinetics. The logistic regression analysis performed in our study showed that embryo quality decreased with age. The pregnancy rate increased significantly with increasing embryo quality.

Insogna et al. [6] concluded that for women with higher BMI, the body habitus causes difficult transfer, hence taking more time, but this did not mean that there will be worse implantation rates. A significant negative association between obesity and live birth was confirmed in a meta-analysis of 682,532 cycles. Obese women have a significantly reduced chance of giving birth following IVF compared to normal BMI women (RR, IC 95%: 0.85, 0.84-0.87). The live birth rate is also significantly lower in overweight women (RR, IC 95%: 0.94, 0.91-0.97) [4]. These results are consistent with a meta-analysis that showed that in 47,967 IVF/ICSI cycles, overweight and obese women had a significantly lower likelihood of clinical pregnancy, and live birth and increased miscarriage rates [21]. Another study showed that when BMI exceeds 29 kg/m², the likelihood of pregnancy per unit was reduced by 4% [22]. Another study found that implantation, clinical pregnancy and live birth rates were significantly reduced in patients with BMI >30.0 kg/m². The adjusted probability ratio of live birth compared with normal-weight cohorts in obese patients was (95% confidence interval [CI]) 0.63 for BMI 30.00-34.99 (0.47-0.85), 0.39 for BMI 35.00-39.99 (0.25-0.61), and 0.32 for BMI ≥40.0 (0.16-0.64). Patients with BMI >30 kg/m² had up to 68% lower live birth rates following the first ART cycle compared to women with BMI <30 [23]. A multicentre retrospective study involving 51,198 women reported that high BMI negatively affected the ongoing pregnancy rate [24]. Maternal obesity may also affect uterine receptivity, according to a retrospective study that looked at the outcomes of 9,587 oocytes donated by normal-weight donors and transferred to women with different BMIs and found that implantation, pregnancy, and live birth rates were lower with higher BMIs [25]. In a retrospective cohort study, clinical pregnancy and live birth rates were found to be

similar in 10.252 frozen-thawed IVF cycles with single blastocyst transfer. However, the risk of miscarriage was found to be higher in obese women compared to women of normal weight. Furthermore, the incidence of preterm birth and C-section delivery rate were found to be elevated in the obese group [26]. However, other studies have not found significant differences in clinical pregnancy rates, miscarriage rates, and live birth rates among different BMI groups [7, 15, 18, 19, 27]. In parallel with these studies, our study found no significant difference between implantation, a positive pregnancy test, and live birth rates.

The limitations of our study include its retrospective design, the absence of a subgroup analysis of the cause of infertility, and the lack of assessment of male obesity. A morphological assessment alone is not enough to rule out aneuploidy. Additionally, our study was limited to a single center. However, the examination of a large number of embryos across all BMI groups enhances the strength and generalizability of our findings.

In conclusion, our retrospective study showed that obese patients had a lower day 5 embryo rate than non-obese patients. No difference was found between BMI and pregnancy rates. It is thought that the reason for the lack of difference may be the low number of patients. Good quality embryo development has a favourable effect on pregnancy outcome, whereas increasing age has a negative effect. The present data suggest that further studies are needed to investigate the mechanism underlying the effect of obesity on embryo development.

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