Original Article

The Effect of Body Mass Index on the Outcome of IVF/ICSI Cycles in Non Polycystic Ovary Syndrome Women

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Abstract

Background: The aim of this study was to investigate the effect of body mass index (BMI) on the outcome of *in vitro* fertilization (IVF)/ intracytoplasmic sperm injection (ICSI) cycles in non polycystic ovary syndrome (PCOs) women.

Materials and Methods: In this cross sectional study, 287 infertile non PCOs women referred to Royan institute, Tehran, Iran between 2002 and 2003 were enrolled. Patients with age≥40 years old or BMI <20 Kg/m^2 were excluded. All of patients underwent IVF or ICSI cycles. The outcome of assisted reproductive technology (ART) were compared between three groups: patients with 20≤ BMI≤25 (normal weight group); patients with 25< BMI≤30 (over weight) and patients with BMI more than 30 Kg/m^2 (obese group). ANOVA, T test, Chi-square and logistic regression were used for analysis.P value less than 0.05 was considered as significant level.

Results: One hundred thirty three (46.3%) subjects had normal BMI, 117 women (40.8%) were overweight and 37 women (12.9%) were obese. Obese group had lower pregnancy rate (13.5%) in comparision to normal (29.3%) and overweight (21.4%) groups although this difference was not statistically significant (p=0.09). Chi square analysis showed that normal weight women had significantly higher regular mensturation (p=0.02). The logestic regression analysis showed that BMI significantly affects on pregnancy rate of ART cycles in non PCOs women (p=0.038).

Conclusion: The finding of this study suggested that in non PCOs women, BMI had independent adverse effect on the pregnancy rate of IVF/ICSI cycles.

Keywords: Body Mass Index, In Vitro Fertilization, Intracytoplasmic Sperm Injection, Outcome, Assisted Reproductive Technology

Introduction

Advancing female age, elevated basal follicle stimulating hormone (FSH) concentrations and extremes of body mass are all believed to have an adverse effect on the outcome of assisted conception cycles (1). Overweight and obesity represents a rapidly growing threat to the health of populations and an increasing number of countries worldwide (2). Significant association are seen in reproductive endocrinology between exess body fat (particularly abdominal obesity) and irregular menstrual cycles, reduced fertility and increased risk of miscarriage (3). It is clearly appears that obesity is associated with an increased risk of hyperandrogenism and anovulation in women in reproductive age as supported by strong association between obesity and the polycystic ovary syndrome (PCOs) (4). Furthermore, obesity especially abdominal obesity ,impairs fecundity and reduces conception rate during infertility treatment (5, 6).Although several studies have performed to evaluate the effect of BMI on IVF/ ICSI outcome (1, 7-11) but there is contraversy.

For this purpose, this study was conducted to evaluate the effect of BMI on the outcome of IVF/ICSI cycles in non PCOs women.

Materials and Methods

In this cross sectional study, 287 infertile non PCOs women referred to Royan institute, Tehran, Iran between 2002 and 2003 were enrolled. This study was approved by ethics committee of Royan institute. All patients signed informed consent form. At first 332 women were included but then in order to omit

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the confounding effect of age , women with age ≥40 years old were excluded from the study (26 women). Also underweight women (women with BMI <20 kg/m^2) were excluded from the study because the percent of underweight women was low among studied patients (only 3.3%) (Fig 1).

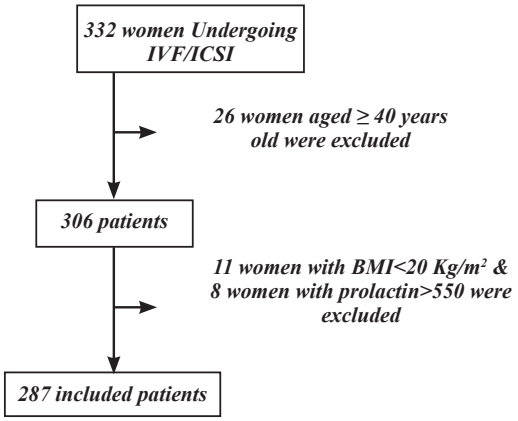

Fig 1: Flow chart of patient selection

Other exclusion criteria consisted of: hypo/hyperthyroidism, hyperprolactinemia & diabetes type 1.
Long standard GnRH agonist protocol was used for ovarian stimulation. In this protocol, the women had first been down regulated with GnRH analogue (Buserline, Hoechst, Germany) which was administered 500 µg/day subcutaneously from 21st day of previous menstrual cycle. When pituitary suppression was achieved (on second day of menstrual cycle, FSH≤ 5 IU/ml, LH ≤5IU/ml, progesterone ≤1ng/ml, Estradiol ≤50pg/ml), Buserline was reduced to 200µg/day and 150-225 IU human Menopausal Gonadotrophin (Menopur, Ferring, Germany) was administrated intramuscularly from 2nd day of menstrual cycle daily. After 3 or more follicles had reached 18 mm in diameter, 10000 IU human Chorionic Gonadotrophin (hCG, Organon, Holland) was used to induce oocyte maturation. Oocytes were aspirated transvaginally with ultrasound guidance 34-36 hour later. After that, IVF or ICSI were done. Uterine embryo transfer was performed two days after oocyte retrieval. Beta hCG was checked two weeks after embryo transfer. Clinical pregnancy was defined as the presence of at least one gestational sac with detectable fetal heart activity by transvaginal sonography. BMI was determined by the ratio of weight divided by the height squared in metric units.
Patients were divided into three subgroups according to BMI (patients with 20≤ BMI ≤25 as normal weight group; patients with 25< BMI ≤30 as over weight and patients with BMI more than 30Kg/m^2 as obese group). SPSS version 11 was used for data entry. T test, ANOVA, Chi-square and logestic regression were used for analysis. Results were presented as mean value±SD. P value less than 0.05 was considered as statistically significant level.

Result

In this study, 287 women were studied. The mean age of women was 29.06±4.58 years old. The mean duration of infertility was 7.04±3.91 years. Two hundred sixty seven patients (93%) had primary infertility. Regular menstrual cycle was seen in 87.1% women . Two hundred thirty cycles (80.1%) were ICSI. Causes of infertility included: male factor (194 cases; 67.6%), female factor (42 subjects; 14.6%), unexplained infertility (24 cases; 8.4%) and both male and female factors (27 cases; 9.4%). Table 1 showes some characteristics of studied women.

Table 1: Characteristics of studied women

Variable	Mean	Standard Deviation
Age(Year)	29.06	4.58
Duration of Infertility (Year)	7.04	3.91
Menstrual Interval (Day)	29.70	3.29
Duration of Menstruation (Day)	6.60	1.38
Serum FSH level on day 3 (IU/ml)	6.38	3. 25

Among studied women,133 women (46.3%) have normal BMI, 117 women (40.8%) were overweight and 37 subjects (12.9%) were obese. Table 2 showes outcome of ART cycles in differenet BMI groups. Clinical pregnancy rate was 29.3% in normal women, 21.4% in overweight and 13.5% in obese women which difference was not statistically significant (p=0.09).

Table 2: Outcome of IVF/ICSI cycles in different BMI groups

Variables	Normal Women (20≤ BMI≤25) (N=133)	Overweight Women (25< BMI≤30) (N=117)	Obese Women (BMI>30) (N=37)	P value
Number of retrieved oocytes	6.57±3.33	6.37±3.51	5.92±3.37	0.58
Number of transferred embryos	3.14±1.20	3.12±1.65	2.97±1.46	0.81
Clinical Pregnancy Rate	39(29.3%)	25 (21.4%)	5 (13.5%)	0.09
Miscarriage Rate	12(9.3%)	14(12.2%)	3(8.1%)	0.2

There were no statistically significant differences in number of retrieved oocytes , transferred embryoes and abortion rate according to different BMI groups. The logestic regression analysis showed that BMI had significantly affect on pregnancy rate (p=0.038) (Table 3).

Table 3: Results of logistic regression analysis

Variable	β	SE	Sig	Exp(B)
BMI	-0.103	0.049	0.038*	0.902

*** p<0.05 was considered as significant level**

Discussion

Detrimental impacts of obesity and overweight on pregnancy and delivary outcomes have long been investigated.Women with obesity and overweight have higher rate of abortion, preterm birth, cesarean delivary and neonatal complications (12). Despite different studies about the effects of obesity and overweight on the outcome of ART cycles, the results of these studies are contraversial.

The present study has demonstrated that increasing in BMI independently of age, FSH, LH, type & duration of infertility affects significantly on the pregnancy rate of IVF/ICSI cycles in non PCOs patients.

The results presented in this study confirm the findings of published studies that have shown an adverse effect on pregnancy outcome in women with high compared with normal BMI [Ku (13), Lintsen (14), Fedorcsak (5, 7), Salha (15), Loveland (8) and Munz's studies (16)] while the result was inconsistency with Lashen (1) , Spandorfer (10) and Dechaud studies (17).

Lintsen et al investigated 8457 women undergoing IVF cycles and found that women with BMI≥ 27 Kg/m^2 had a significantly lower delivery rate [OR=0.67; 95%(CI)=0.48-0.94] compared with normal weight (14). In one research, Fedorcsak et al studied 383 patients conceiving after IVF or ICSI and found that obese group (BMI>25 Kg/m^2) had higher abortion rate during the first 6 weeks and lower live birth rate (5). In another study , they evaluated records of 5019 IVF/ICSI treatments in 2660 couples .In their recent study, they considered patients with BMI>30 Kg/m^2 as obese group and showed that obesity was associated with lower chances for live birth after IVF/ICSI (7). Salha et al studied fifty patients with a high BMI (≥26Kg/m^2) in comparison to 50 patients with normal BMI (18-25) undergoing IVF cycles. They showed that clinical pregnancy rate per cycle was statistically lower in the patients with high BMI (15). Loveland et al evaluated 139 women <40 years old undergoing IVF. Their finding showed that in patients with BMI>25, pregnancy rate was statistically lower while spontaneous miscarriage was slightly higher (8) .Munz et al compared 28 patients with BMI<25 and 24 patients with BMI>25 undergoing IVF /ICSI. They showed that pregnancy rate was higher in women with BMI<25 although this difference was not significant (16).

In contrast, Lashen et al compared 76 obese women (BMI>27.9) with 152 controls and 35 underweight women (BMI<19) with 70 controls .They found that the clinical pregnancy and miscarriage rates were not significantly different from their controls and concluded that the extremes of BMI do not adversely affect the outcome of IVF treatment (1). Dechaud et al in their retrospective study, classified patients in four groups: BMI<20; 20≤BMI<25; 25 ≤BMI<30 and BMI≥30. They concluded that obesity does not negatively affect on results of IVF/ICSI cycles (17).

The mechanism explaining the effect of BMI on pregnancy outcome is uncertain. Ku et al in their study on 164 patients under 37 years showed that no difference in the endometrial thickness were seen in different BMI groups (with cutoff 24Kg/m^2) and suggested that BMI affect ovarian folliculogenesis rather than uterine receptivity (13). Accordance to this assumption, in present study, fewer retrieved oocytes were seen in obese group in comparison with normal & over weight subjects although this finding was not statistically significant. This finding was similar to Ku (13), Fedorcsak (5, 7), Salha (15), Wittmer (11) and Spandorfer (10) although all of them except ku, found statistically decrease in number of retrieved oocytes in obese groups. Inconsistency with these studies, Lashen (1) and Frattarelli (9) did not found this effect on retrieved oocytes in obese group. Wittmer et al analyzed 398 couples and categorized them according to their BMI (BMI<20; 20≤BMI<25 and BMI≥25 Kg/m^2). They found that the number of collected oocytes decreased when BMI was ≥25 Kg/m^2 (11). Spandorfer et al evaluated 920 patients (<40 years old). They considered BMI >27 as obese group. They revealed that obese patients had fewer oocytes retrieved. Despite this, the clinical pregnancy rate (per retrieval) had no difference in obese and non obese patients (10).

Conclusion

Increasing in BMI has detrimental significant effect on outcome of IVF/ICSI cycles. Further studies in a larger scale are necessary to search the underlying mechanisms and to evaluate the effects of BMI in older women & in subjects using other COH protocols.

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References
1. Lashen H, Ledger W, López Bernal A and Barlow D. Extremes of body mass do not adversely affect the outcome of superovulation and in-vitro fertilization. Hum Reprod. 1999 ;14(3): 712-715.
2. World Health Organization. Preventing and managing the global epidemic. Report of a WHO consultation on obesity. Geneva, WHO 1997.
3. Pasquali R, Casimirri F, Cantobelli S, Labate AM, Venturoli S, Paradisi R, et al. Insulin and androgen relationships with abdominal body fat distribution in women with and without hyperandrogenism. Horm Res. 1993; 39(5-6): 179-187.
4. Pasquali R, Pelusi C, Genghini SL, Cacciari M, Gambineri A. Obesity and reproductive disorders in women. Hum Reprod Update. 2003; 9(4): 359-372.
5. Fedorcsak P, Storeng R, Dale PO, Tanbo T, Abyholm T. Obesity is a risk factor for early pregnancy loss after IVF or ICSI. Acta Obstet Gynecol Scand. 2000; 79(1): 43-8.
6. Wass P, Waldenstrom U, Rossner S, Hellberg D. An android body fat distribution in females impairs the pregnancy rate of in-vitro fertilization-embryo transfer. Hum Reprod. 1997; 12(9): 2057-2060.
7. Fedorcsak P, Dale PO, Storeng R, Ertzeid G, Bjercke S, Oldereid N, et al. Impact of overweight and underweight on assisted reproduction treatment. Hum Reprod. 2004; 19(11): 2523-2528.
8. Loveland JB, McClamrock HD, Malinow AM, Sharara FI. Increased body mass index has a deleterious effect on in vitro fertilization outcome. J Assist Reprod Genet. 2001; 18(7): 382-386
9. Frattarelli JL, Kodama CL. Impact of body mass index on in vitro fertilization outcomes. J Assist Reprod Genet. 2004; 21(6): 211-215.
10. Spandorfer SD, Kump L, Goldschlag D, Brodkin T, Davis OK, Rosenwaks Z. Obesity and in vitro fertilization: negative influences on outcome. J Reprod Med. 2004; 49(12): 973-977.
11. Wittemer C, Ohl J, Bailly M, Bettahar-Lebugle K, Nisand I.Does body mass index of infertile women have an impact on IVF procedure and outcome? JAssist Reprod Genet. 2000; 17(10): 547-552.
12. Isaacs JD, Magann EF, Martin RW, Chauhan SP, Morrison JC. Obstetric challenges of massive obesity complicating pregnancy.J Perinatol. 1994; 14(1): 10-14.
13. Ku SY, Kim SD, Jee BC, Suh CS, Choi YM, Kim JG, et al. Clinical efficacy of body mass index as predictor of in vitro fertilization and embryo transfer outcomes. J Korean Med Sci. 2006; 21(2): 300-303.
14. Lintsen AM, Pasker-de Jong PC, de Boer EJ, Burger CW, Jansen CA, Braat DD, et al. Effects of subfertility cause, smoking and body weight on the success rate of IVF. Hum Reprod. 2005; 20(7): 1867-1875.
15. Salha O, Dada T, Sharma V. Influence of body mass index and self-administration of hCG on the outcome of IVF cycles: a prospective cohort study. Hum Fertil (Camb). 2001; 4(1): 37-42.
16. Munz W, Fischer-Hammadeh C, Herrmann W, Georg T, Rosenbaum P, Schmidt W, et al. Body mass index, protein metabolism profiles and impact on IVF/ICSI procedure and outcome. Zentralbl Gynakol. 2005; 127(1): 37-42.
17. Dechaud H, Anahory T, Reyftmann L, Loup V, Hamamah S, Hedon B . Obesity does not adversely affect results in patients who are undergoing in vitro fertilization and embryo transfer. Eur J Obstet Gynecol Reprod Biol. 2006; 127(1): 88-93.