

Effect of Weight Loss in Morbidly Obese Infertile Women on IVF Outcome

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Abstract

Background: Morbid obesity is associated with a lower chance of pregnancy *via* IVF treatment. As a result many IVF programs have restricted this treatment to women with a BMI of <35 kg/m² and recommend weight loss for morbidly obese women (MOW). The purpose of this study is to analyze the effect of weight loss to a BMI <35 kg/m² and its result on the IVF treatment outcome.

Methodology: Retrospective cohort study where MOW with primary infertility and one previous unsuccessful IVF treatment cycle were included. They were advised to lose weight in the span of a year and restart IVF treatment. Women who managed to reduce their BMI to <35 kg/m² were considered as Group A and women who did not reduce their BMI to <35 kg/m² were considered as Group B.

Result: Twenty-seven women successfully reduced their weight and underwent 49 IVF cycles in Group A. The remaining 65 MOW underwent 108 IVF cycles in Group B. Patients in Group A were younger and had better stimulation characteristics. The difference in pregnancy rate per started cycle did not reach statistical significance.

Conclusion: Modest weight loss to a BMI <35 kg/m² through diet and exercise, a method that requires time and effort, is more easily achieved by younger patients but does not increase the pregnancy rate in IVF treatment cycles.

Keywords: IVF; Morbid obesity; Obesity; Weight loss

Introduction

Obesity is a common condition in the Saudi population [1,2]. It is estimated that around 40% of Saudi females at the reproductive age suffer from obesity, moreover obesity is associated with many health problems [3,4]. A higher prevalence of obesity among infertile

women was also found, likely due to polycystic ovarian syndrome, hyperandrogenism and hyperinsulinemia being linked to both obesity and infertility [5,6].

The National Institute of Health (NIH) begins to categorize a patient as 'obese' at the body mass index (BMI) >30 kg/m², then further categorizes obesity into; Class I with BMI= 30-34.9 kg/m², Class II with BMI= 35-39.9kg/m² and Class III with BMI >40 kg/m² [7].

The effect of obesity on pregnancy and IVF outcome has been previously studied with findings showing that obesity increases cancellation of IVF cycles, causes poor response to treatment [8,9], and lowers the chances of live birth [10-12]. Obesity was also proven to be associated with an increased risk of first trimester abortion and recurrent miscarriage [13]. As a result multiple IVF programs placed an arbitrary cut off for accepting IVF patients who have a BMI >35 kg/m² [14].

Although Class II and Class III patients are encouraged to lose weight before their infertility treatment, there are conflicting reports on the effect of weight loss on reproductive outcome [15-17]. These studies included women with BMIs >29 kg/m², but the actual IVF outcome in morbidly obese infertile women before and after weight loss has never been compared. The objective of this study is to assess the effect of weight loss on IVF outcome in the morbidly obese population following the change in their obesity from Class II and III to Class I.

Materials and Methods

The study is a retrospective cohort study. Patients included in the study were patients who participated in an earlier study at the same center and did not achieve pregnancy [18]. These are women between 20 and 40 years old with primary infertility and who had an unsuccessful IVF cycle while their BMI was ≥ 35 kg/m². They had extensive counseling and referral to a dietitian for weight loss aiming to drop their BMI to <35 kg/m². Patients who managed to achieve the expected weight loss and had an IVF cycle were considered as the study group (group A). The other group of patients who did not drop their BMI to <35 kg/m² and had subsequent IVF treatment was considered as the control group (group B). The primary outcome was the clinical pregnancy rate per started cycle. Patients with a positive pregnancy test 2 weeks post-embryo transfer were considered pregnant, those patients would then have a transvaginal ultrasound at 5 weeks post-embryo transfer to check for fetal viability. Clinical

pregnancy was defined as pregnancy with positive heartbeat seen by transvaginal ultrasound scan at 5 weeks post-embryo transfer. Other secondary outcomes such as cycle cancellation, the needed dose of human menopausal gonadotropin, the number of oocytes retrieved, the fertilization rate, the number of embryos transferred and the rate of ovarian hyperstimulation syndrome were also compared between the two groups. Moreover, Group A's post-weight loss parameters were compared to their pre-weight loss data.

IVF treatment protocol was described in the past [18]. Statistical analysis was performed using S-plus 2000. Two-tailed t-test was used for parametric data, Mann-Whitney test was used for non-parametric data, and Chi-square test was used for binomial data. A p value of < 0.05 was considered statistically significant. Paired analysis was used as needed.

Results

There were 92 morbidly obese women who fulfilled the inclusion criteria and 27 of them reduced their weight to a BMI <35 kg/m² (Class I obesity). They underwent a total of 49 IVF cycles (Group A). The remaining 65 women remained Class II or III obesity and underwent 108 IVF cycles (Group B). Both groups had similar diagnostic categories and height (Table 1). As expected, the patients who managed to lose weight had significantly lower BMI and weight. Additionally, they were significantly younger compared to the patients who failed to lose weight (Table 1).

Patient who achieved the target weight loss required lower doses of HMG, had more follicles, higher number of oocytes retrieved and had a higher fertilization rate (Table 1). The length of stimulation and the number of embryos transferred were similar in both groups. The difference in pregnancy rate per started cycle did not reach statistical significance.

Patients who achieved the desired weight loss (Group A) had significantly lower cancellation rate per started cycle compared to Group B (Table 1). The cancellation rate for group B was 21.3%. Out of a total 23 cancelled cycles in Group B, nine were prior to ovum pick up (seven due to poor response, one for risk of OHSS, and one due to no sperms found in the male procedure). The remaining fourteen cycles in group B were cancelled following oocyte retrieval (one developed early OHSS, and the other thirteen were either for lack of fertilization or due to arrested embryo division). Group A had only three cancellations (6.1%), two of them prior to the OPU (one for risk of OHSS, and one due to no sperms in the male procedure sample). The third cancellation was following oocyte retrieval due to lack of fertilization.

We compared the IVF outcome of those 27 women in Group A after weight reduction to their outcome prior to weight loss and as expected they had significantly lower BMI and weight following weight loss advice (Table 2). There was an average of 10% weight reduction after the diet and exercise. Table 2 shows pre and post weight reduction IVF cycle parameters for Group A patients, and it can be noted that there were significantly lower cancellation rates following weight reduction.

Discussion

As obesity is becoming a major health concern in the world [3,4], its implication on reproductive health and effect on infertility treatment has also been investigated [19-24]. It has been reported that pregnancy rate significantly decreases with increasing BMI [24].

Table 1: Patient and cycle characteristics

	Group A (n=49 cycles)	Group B (n=108 cycles)	P
Age (years)	31.4 ± 5	34.7 ± 5.	0.001
BMI (kg/m ²)	33.1 ± 1.3	37.9 ± 2.4	0.001
WT (kg)	80 ± 6.7	90.4 ± 7.7	0.001
Ht (cm)	156 ± 5.4	154.6 ± 5.5	NS
ICSI n (%)	87%	83%	NS
Male factor n (%)	(29) 59%	(76) 70%	NS
Unexplained infertility n (%)	(4) 8%	(9) 8%	NS
Tubal Factor n (%)	(16) 33%	(23) 22%	NS
Number of follicles	17 ± 7.4	11.4 ± 6.7	0.001
Number of oocyte collected	10.6 ± 5.3	7.1 ± 4.5	0.001
2PN	5.7 ± 3.9	3.6 ± 2.9	0.004
Number of embryos	5.2 ± 3.5	3.2 ± 2.5	0.01
Number of embryos transferred	1.97 ± 0.45	1.58 ± 0.8	0.01
Length of stimulation	12.6 ± 3.3	13.1 ± 4.1	NS
Dose of HMG	37.3 ± 11.8	49.4 ± 16.9	0.01
Cancellation rate n (%)	6.10%	21.30%	0.03
Pregnancy rate per started cycle	15 (30.6%)	28 (25.9)	NS
Clinical pregnancy rate per started cycle	11 (22.45%)	20 (18.5%)	NS

This study aimed to look at a common problem in IVF practice; the approach to morbidly obese women in IVF programs. While data is not consistent in regard to the negative effect of obesity on implantation rate or live birth rate in IVF treatment [15-17], many programs still place a limit on patient's access to IVF treatment based on their BMI and are supported by certain societies' guidelines [14,25]. Tremellen et al. recently reviewed the scientific and ethical aspects of such practices which block the access of care for certain patients and concluded that there was no scientific support for this suggestion, stating that "This prohibition is particularly unjust when IVF is the only treatment capable of producing a pregnancy" [26].

Although large data sets suggested that high BMIs carry a negative effect on the pregnancy rate in IVF treatment cycles, causing these programs to place an arbitrary line for including patients in their treatment eligibility, there is no sufficient evidence to support that reducing patients' weight below that line would improve their pregnancy rate [27-29].

In this study, the women who had tried to lose weight through diet and exercise were 2 years older (on average) at the time they reduced their BMI to the desired level. Although there was significant improvement on the secondary cycles stimulation parameters such as cancellation rate, which could be the reflection of the improvement in the number and quality of oocytes retrieved as reported by other

Table 2: Comparison of Pre and Post Weight Loss Parameters

	Group A (Post Wt Reduction)	Group A (Pre Wt Reduction)	P
Age (years)	31.4 ± 5	29.9 ± 6	NS
BMI (kg/m ²)	33.1 ± 1.3	36.6 ± 2	0.01
WT (kg)	80 ± 6.7	88.5 ± 10	0.01
Number of follicles	17 ± 7.4	16 ± 11	NS
Number of oocyte collected	10.6 ± 5.3	12 ± 12	0.01
Number of fertilized oocytes	5.7 ± 3.9	4.9 ± 4.9	NS
Number of embryos at day 3	5.2 ± 3.5	4.1 ± 4.6	NS
Number of embryos transferred	1.97 ± 0.45	1.4 ± 1.1	0.01
Length of stimulation	12.6 ± 3.3	14.7 ± 2.9	NS
Dose of HMG (ampules)	37.3 ± 11.8	38.6 ± 12.1	NS
Cancellation rate (%)	6.10%	28%	0.01

authors [30,31], this was not translated to significantly improve the pregnancy rate following modest weight loss by diet and exercise in morbidly obese women. One can argue that the relatively limited sample size may play a role in not showing a statistical difference in the pregnancy outcome among the groups.

Our data in this study is in concordance with other recently published data [15,17], and further analysis of a large prospective randomized control study did not identify any subgroup to benefit from the lifestyle intervention [32]. While data on bariatric surgery and IVF outcome is still limited, the increasing popularity of this procedure will give an interesting opportunity to see more data on their effect-especially in patients with very high BMI [33,34].

Since the process of weight loss by the diet and exercise method takes time and effort, we might be jeopardizing patients' outcome by delaying their treatment until they are in older age groups. One must calculate the risks to the potential benefits from the weight loss method on the pregnancy rate.

We concluded from this study that modest weight loss to BMI <35 kg/m² by diet and exercise is more easily achieved by younger patients but does not increase the pregnancy rate in IVF treatment cycles, we also recommend the review of any policy restricting patient access to IVF treatment based on their BMI.

Ethics

This project was approved by the ethical committee of the research advisory council (RAC) at King Faisal Hospital & Research Center, Riyadh, Saudi Arabia, with RAC number 2061032. This research followed the ethical principles of research projects involving humans in compliance with the Helsinki Declaration. As retrospective study the ethical committee waived the need for written consent from participants.

Conflict of Interest

The authors declare that they have no competing interests.

References

- Hamilton CJ, Jaroudi KA, Sieck UV (1995) High Prevalence of Obesity in a Saudi Infertility Population. *Ann Saudi Med* 15: 344-346.
- Rahim HF, Sibai A, Khader Y, Hwalla N, Fadhil I, et al. (2014) Non-communicable diseases in the Arab world. *Lancet* 383: 356-367.
- Al-Nozha MM, Al-Mazrou YY, Al-Maatouq MA, Arafah MR, Khalil MZ, et al. (2005) Obesity in Saudi Arabia. *Saudi Med J* 26: 824-829.
- Daoud F, El Bcheraoui C, Tuffaha M, Al Mazroa M, Al Saeedi M, et al. (2016) The health status of Saudi women: findings from a national survey. *J Public Health (OXF)* 38: 660-672.
- Cui N, Wang H, Wang W, Zhang J, Xu Y, et al. (2016) Impact of Body Mass Index on Outcomes of In Vitro Fertilization/Intracytoplasmic Sperm Injection Among Polycystic Ovarian Syndrome Patients. *Cell Physiol Biochem* 39: 1723-1734.
- Norman RJ, Noakes M, Wu R, Davies MJ, Moran L, et al. (2004) Improving reproductive performance in overweight/obese women with effective weight management. *Hum Reprod Update* 10: 267-280.
- The practical guide (2000) Identification, evaluation and treatment of overweight and obesity in adults. Bethesda (MD): National Institutes of Health, National Heart, Lung and Blood Institute, North American Association for the Study of Obesity 1-88.
- Spandorfer SD, Kump L, Goldschlag D, Brodtkin T, Davis OK, et al. (2004) Obesity and in vitro fertilization: negative influences on outcome. *J Reprod Med* 49: 973-977.
- Frattarelli JL, Kodama CL (2004) Impact of body mass index on in vitro fertilization outcomes. *J Assisted Reprod Gen* 21: 211-215.
- Fedorcsák P, Dale PO, Storeng R, Ertzeid G, Bjercke S, et al. (2004) Impact of overweight and underweight on assisted reproduction treatment. *Hum Reprod* 19: 2523-2528.
- Clark AM, Thornley B, Tomlinson L, Galletley C, Norman RJ (1998) Weight loss in obese infertile women results in improvement in reproductive outcome for all forms of fertility treatment. *Hum Reprod* 13: 1502-1505.
- Lintsen AM, Pasker-de Jong PC, de Boer EJ, Burger CW, Jansen CA, et al. (2005) Effects of subfertility cause, smoking and body weight on the success rate of IVF. *Hum Reprod* 20: 1867-1875.
- Lashen H, Fear K, Sturdee DW (2004) Obesity is associated with increased risk of first trimester and recurrent miscarriage: matched case-control study. *Hum Reprod* 19: 1644-1646.
- Balen AH, Anderson RA (2007) Impact of obesity on female reproductive health: British Fertility Society, Policy and Practice Guidelines. *Hum Fertil* 10: 195-206.
- Einarsson S, Bergh C, Friberg B, Pinborg A, Klajnbard A, et al. (2017) Weight reduction intervention for obese infertile women prior to IVF: a randomized controlled trial. *Hum Reprod* 32: 1621-1630.
- Sim KA, Dezarnaulds GM, Denyer GS, Skilton MR, Caterson ID (2014) Weight loss improves reproductive outcomes in obese women undergoing fertility treatment: a randomized controlled trial. *Clin Obes* 4: 61-68.
- Mutsaerts MA, van Oers AM, Groen H, Burggraaff JM, Kuchenbecker WK, et al. (2016) Randomized Trial of a Lifestyle Program in Obese Infertile Women. *N Engl J Med* 374: 1942-1953.
- Awartani KA, Nahas S, Al Deery M, Coskun S, Al Hassan S (2009) Infertility treatment outcome in sub groups of obese population. *Reprod Biol Endocrinol* 27: 7-52.

19. Kresowik J, Sparks A, Van Voorhis B (2012) Clinical factors associated with live birth after single embryo transfer. *Fertil Steril* 98: 1152-1156.
20. Dessolle L, Freour T, Ravel C, Jean M, Colombel A, et al. (2011) Predictive factors of healthy term birth after single blastocyst transfer. *Hum Reprod* 26: 1220-1226.
21. Dessolle L, Darai E, Cornet D, Rouzier R, Coutant C, et al. (2009) Determinants of pregnancy rate in the donor oocyte model: a multivariate analysis of 450 frozen-thawed embryo transfers. *Hum Reprod* 24: 3082-3089.
22. Petanovski Z, Dimitrov G, Ajdin B, Hadzi-Lega M, Sotirovska V, et al. (2011) Impact of body mass index (BMI) and age on the outcome of the IVF process. *Prilozi* 32: 155-171.
23. Pinborg A, Gaarslev C, Hougaard CO, Nyboe Andersen A, Andersen PK, et al. (2011) Influence of female body weight on IVF outcome: a longitudinal multicentre cohort study of 487 infertile couples. *Reprod Biomed Online* 23: 490-499.
24. Rittenberg V, Seshadri S, Sunkara SK, Sobaleva S, Oteng-Ntim E, et al. (2011) Effect of body mass index on IVF treatment outcome: an updated systematic review and meta-analysis. *Reprod Biomed Online* 23: 421-439.
25. Robson S (2014) Ovarian stimulation in assisted reproduction. The Women's Health Committee and approved by the RANZCOG Board and Council.
26. Tremellen K, Wilkinson D, Savulescu J (2017) Should limited? A scientific obese women's access to assisted fertility treatment be and ethical analysis. *Aust N Z J Obstet Gynaecol* 57: 569-574.
27. Bellver J, Pellicer A, García-Velasco JA, Ballesteros A, Remohí J, et al. (2013) Obesity reduces uterine receptivity: clinical experience from 9,587 first cycles of ovum donation with normal weight donors. *Fertil Steril* 100: 1050-1058.
28. Provost MP, Acharya KS, Acharya CR, Yeh JS, Steward RG, et al. (2016) Pregnancy outcomes decline with increasing body mass index: analysis of 239,127 fresh autologous *in vitro* fertilization cycles from the 2008-2010 Society for Assisted Reproductive Technology registry. *Fertil Steril* 105: 663-669.
29. Provost MP, Acharya KS, Acharya CR, Yeh JS, Steward RG, et al. (2016) Pregnancy outcomes decline with increasing recipient body mass index: an analysis of 22,317 fresh donor/recipient cycles from the 2008-2010 Society for Assisted Reproductive Technology Clinic Outcome Reporting System registry. *Fertil Steril* 105: 364-368.
30. Wu LL, Norman RJ, Robker RL (2011) The impact of obesity on oocytes: evidence for lipotoxicity mechanisms. *Reprod Fertil Dev* 24: 29-34.
31. Shah DK, Missmer SA, Berry KF, Racowsky C, Ginsburg ES (2011) Effect of obesity on oocyte and embryo quality in women undergoing *in vitro* fertilization. *Obstet Gynecol* 118: 63-70.
32. van Oers AM, Groen H, Mutsaerts MA, Burggraaff JM, Kuchenbecker WK, et al. (2016) Effectiveness of lifestyle intervention in subgroups of obese infertile women: a subgroup analysis of a RCT. *Hum Reprod* 31: 2704-2713.
33. Milone M, Sosa Fernandez LM, Sosa Fernandez LV, Manigrasso M, Elmore U, et al. (2017) Does Bariatric Surgery Improve Assisted Reproductive Technology Outcomes in Obese Infertile Women? *Obes Surg* 27: 2106-2112.
34. Tan O, Carr BR (2012) The impact of bariatric surgery on obesity-related infertility and *in vitro* fertilization outcomes. *Semin Reprod Med* 30: 517-528.