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Effect of Body Mass Index on in Vitro Fertilization Outcomes

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Abstract: ***Introduction: Several factors can affect the outcomes of IVF, such as maternal age, ovarian reserve, and the quality of embryos. Recently, there has been growing evidence that suggests body mass index (BMI) could also influence the success rates of IVF. BMI is a measure of body fat based on height and weight and has been associated with several health problems, including infertility. However, the exact correlation between BMI and IVF outcomes is still under investigation. Materials and methods: This was a retrospective research done on infertile women who underwent IVF at Madras Medical Mission and were IRM OPD patients. The 220 women who underwent IVF therapy between 2018 and 2021 were included in the study, and their BMI was noted at the start of the procedure. They included AMH, AFC, FSH, luteinizing hormone (LH), and estradiol (E2). All of the study's participants experienced antagonist protocol - controlled ovarian hyper stimulation. Results: 42 people (19.1%) were in the normal weight range, 90 people (40.9% were overweight), and 71 people (32.3%) were obese. Regarding age, the length of infertility, and both female and male causes of infertility, all three groups were comparable. Day 2 LH/FSH levels, endometrial thickness, gonadotrophin needs, oocyte quality, fertilisation, cleavage rates, number of good quality embryos, and clinical pregnancy rates were all comparable between the three groups. Conclusion: Increased body mass index in women does not seem to have a negative impact on the success of IVF. Nonetheless, preconception counselling for obese women is essential because losing weight lowers the risk of problems associated to pregnancy.***

Keywords: Obesity, Subfertility, Invitro - fertilization, Body mass index

1. Introduction

In vitro fertilization (IVF) is a popular assisted reproductive technology used for treating infertility in couples. The success of IVF treatment depends on various factors, including the age, cause of infertility, and body mass index (BMI) of the female partner. BMI is a measure of body fat based on height and weight and is commonly used to assess the health status of individuals. Recent studies have suggested that high BMI may negatively impact the outcomes of IVF treatment.[1- 3] Therefore, it is important to investigate the correlation between BMI and IVF outcomes to improve the success rate of IVF treatment.

Obesity is becoming a fast growing health problem across the world. Obesity impacts a broad array of health risks in women across the lifespan[4], including adverse reproductive health outcomes such as menstrual cycle irregularity, abnormal uterine bleeding, endometrial hyperplasia, infertility, and pregnancy complications.[5 - 9]

In assisted reproduction, however, there are conflicting reports on the effect of obesity on oocyte quality, embryo development, and lower number of mature oocytes, lower implantation and pregnancy rates.[10]

However, even women with obesity and regular menstrual cycles exhibit a longer time to spontaneous pregnancyand lower success rates of controlled ovarian hyperstimulation compared to their normal - weight counterpart.[12]Despite strides toward characterizing the nature of reproductive disturbances in obesity, several questions remain to be answered on how and why obesity may drive disordered ovarian function.

Several studies have been conducted to evaluate the impact of BMI on IVF outcomes. Some studies have suggested that women with high BMI have a lower chance of getting pregnant after IVF treatment than women with normal BMI. Additionally, high BMI has been associated with a higher risk of miscarriage, gestational diabetes, pre - eclampsia, and other pregnancy - related complications. However, some studies have reported conflicting results, and the exact relationship between BMI and IVF outcomes is still not clear. With this background, we conducted this study with objective to assess the effect of women's BMI on the oocyte/embryo quality and the reproductive outcome of our non - donor IVF/ICSI cycles.

2. Methodology

After receiving approval from the institutional ethical committee, a retrospective study of medical records of women who have undergone non donor IVF cycles in IRM from January 2018 to December 2021 was conducted.

The sample size was calculated by using using Medcalcsoftware. Formula used: $N = (1.96)\ ^2p \times q/d^2$. (p =16.5, q= 100 - p, d = 5). At 95% confidence level, 80% power of the study, absolute precision of 5% and the prevalence of live birth rate among obese women as 16.5% according to study by A Nicoletti et. al.1[6]The calculated sample size was 220.

The study was conducted among sub - fertile patients of age between 21 - 40 years, who have undergone IVF at Institute of Reproductive health.

a) **Inclusion Criterion**: All Sub fertile patients of age between 21 - 40 years, who underwent IVF at Institute of Reproductive health.
b) **Exclusion Criterion:**
   - Severe endometriosis
   - Severe male factor infertility.
   - Oocyte donors
   - Women with known history of poor oocytes.

The study population was classified into four groups based on BMI according to WHO classification.
1) Under weight (BMI <18.5kg/m2)
2) Normal weight (BMI 18.5 - 24.9 kg/m2)
3) Overweight (BMI 25 - 29.9 kg/m2)
4) Obese (BMI>30 kg/m2)
   - Obese class I (30.0 - 34.9kg/m^2)
   - Obese class II (35.0 - 39.9kg/m^2)
   - Obese class III (≥ 40kg/m^2)

The subfertile women case files were evaluated and AMH levels and AFC count were noted. Day two of hormonal evaluations (serum follicle stimulating hormone (FSH), luteinizing hormone (LH), and estradiol (E2)) were also noted. All women included in the study had underwent controlled ovarian hyper stimulation using antagonist protocol. IVF stimulation was started on second day of cycle using HMG, recombinant FSH or highly purified HMG (150 - 450IU/ day). Standard fixed antagonist protocol started from day 5 of stimulation. Trigger was given using HCG alone or in selected patients with dual trigger - HCG and GnRH agonist (Triptorelin). Oocyte retrieval was done 35 hours after trigger. The number of oocytes retrieved and their quality assessed and noted.

The 6 individual parameters of oocytes will be assessed as follows to grade their quality:

Parameter	Good Quality	Average Quality	Poor Quality
Oocyte morphology	Normal oocyte coloration, round shape	Less dark general oocyte coloration and less ovoid shape	Dark general oocyte coloration and/or ovoid shape
Oocyte size	>130µm and <150 µm	Size did not deviate from normal by >10 µm	Size <120 µ or greater 160 µm
Ooplasm	Absence of granularity and inclusions	Slightly granular and/or demonstrated only few inclusions	Very granular and/or very vacuolated and/or demonstrated several inclusions.
PVS	Normal size PVS with no granules	Moderately enlarged PVS and/or small PVS and/or less granular PVS	Abnormally large PVS, an absent PVS or a very granular PVS
Zona pellucida	Normal zona (>12 µm and <18 µm)	Did not deviate from normal by >2 µm	Very thin or thick (<10 µm or>20 µm)
Polar body	Round shape and clear borders	Fair but not excellent	Flat and/or multiple PBs, granular and/or either abnormally small or large PBs.

The clinical pregnancy rates were noted among these patients. All data were entered in Microsoft excel and statistical analysis was performed using the statistical software SPSS version 21.0.

3. Results

We divided the study participants into three groups.
Group 1 (N= 42): Normal weight - BMI 18.5 - 24.9 kg/m^2
Group 2 (N= 90): Overweight - BMI 25 - 29.9 kg/m^2
Group 3 (N= 71): Obese BMI>30 kg/m^2

Table 1: Baseline characteristics among study groups

		Group 1	Group 2	Group 3	P value
Age (Mean±SD)		32.5±3.9	31.88±4.5	31.99±4.1	0.729
Cycle number		1.43±0.89	1.36±0.66	1.39±0.75	0.8798
Gonadotropin dose (IU)		3658.61±1110.8	3399.8±1029.5	3568.54±1146.86	0.387
Days of STI		10.48±0.71	10.6±0.7	10.59±0.89	0.688
Type of infertility	Female	18 (42.9%)	76 (84.4%)	58 (81.7%)	0.563
	Male	1 (2.4%)	3 (3.3%)	1 (1.41%)	
	Both	6 (14.3%)	11 (12.2%)	12 (16.9%)	
Trigger	Hcg	16 (38.1%)	52 (57.8%)	41 (57.7%)	0.041
	Decapeptyl	1 (2.4%)	8 (8.9%)	3 (4.2%)	
	Both	25 (5.6%)	30 (33.3%)	27 (38.03%)	

Table 1 shows the comparison of baseline characteristics among three study groups. We found no significant differences in terms of age, cycle number, gonadotropin dose, days of stimulation and type of infertility among the three study groups (p>0.05). There was significant difference in terms of trigger used among three groups (p<0.05), dual trigger was used maximum in group 3 (obese) in comparison to other groups.

Table 2: Day 2 AMH, AFC, LH, E2 and FSH in the three groups

	Group 1	Group 2	Group 3	P value
AMH (ng/ml)	2.69±1.32	2.67±1.59	2.99±2.28	0.521
AFC	14.71±7.99	14.2±7.73	15.06±8.13	0.503
LH (mIU/ml)	4.01±1.63	4.25±2.33	3.56±1.57	0.086
E2 (pg/ml)	29.62±8.43	30.2±9.33	30.85±11.31	0.808
FSH (ng/ml)	6.29±1.28	6.07±2.45	5.95±2.18	0.722

Table 2 shows that there was no significant difference between the three groups in terms of day 2 AMH, AFC, LH, E2 and FSH levels are concerned (p>0.05). There was mild increase in AMH among obese group patients. There is also a mild increase in number of AFCs in group 3 (obese group) but no statistical analysis.

Table 3: Comparison of number of follicles, oocytes and embryos in the three groups

	Group 1	Group 2	Group 3	P value
Number of follicles	10.07±5.77	10.2±4.95	10.54±6.71	0.898
Number of oocytes	10.19±6.56	10.51±5.2	10.45±6.91	0.961
Number of M2	8.76±5.95	8.99±4.51	8.39±5.05	0.753
Number of Embryos	8.14±5.97	8.87±8.99	7.66±4.96	0.565
Number of embryos transferred	3.12±0.84	2.74±0.84	2.65±0.90	0.023
Number of embryos cryopreserved	8.10±5.82	7.76±4.26	7.44±4.74	0.773

Table 3 shows, There was no difference based on number of follicles, oocytes, M2 oocytes and embryos, no of embryos transferred or cryopreserved among the three study groups. (p>0.05)

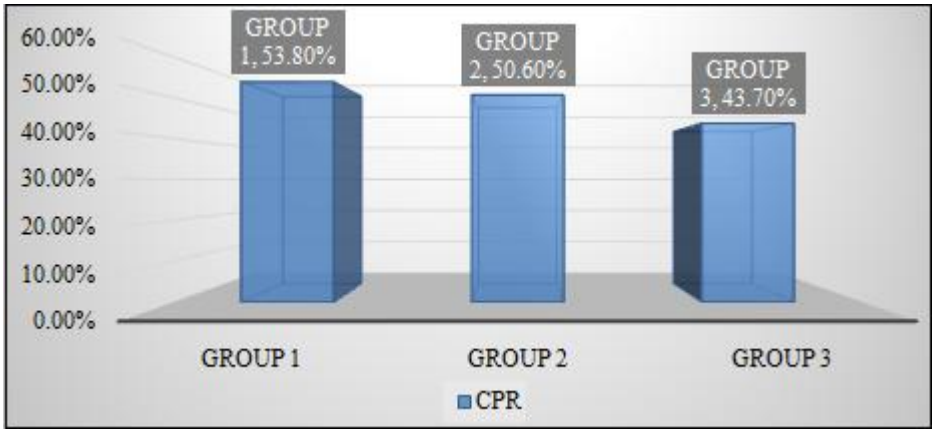

Figure 1: Comparison of outcome in the three groups

Figure 1: Shows that the clinical pregnancy rate was higher in group 1 (normal weight) and group 2 (over weight) in comparison with group (obese), but there was no statistical significance (p>0.05)

Table 4: Comparison of outcome in obese women

Outcome	Group 3			P value
	BMI: 30 to 34.9 Obese class I	BMI: 35 to 39.9 Obese class II	BMI: >40 Obese class III	
CPR	27 (45.8%)	3 (42.8%)	1 (20%)	0.536
No pregnancy	32 (54.2%)	4 (57.2%)	4 (80%)	
Total	59 (100%)	7 (100%)	5 (100%)	-

Table 4 shows the outcome of women in obese women who belonged to group 3 and we found that clinical pregnancy rate was higher in patients with obese class 1 but no statistical significance was present. (p>0.05)

4. Discussion

Subfertility in obese women has been mostly caused by anovulatory failure.1[7] Normal cycling obese women have also been reported to have lower conceiving rates (5% every unit increase in BMI beyond 29 kg/m2). It is debatable how BMI affects obese women receiving regulated ovarian stimulation.[10, 12, 15, 17]

Our research demonstrates that BMI has no negative effects on the success of IVF. In all three groups, regardless of weight, the blood hormone parameters (day 2 gonadotrophin values, estradiol levels on hCG day) were comparable. Considering that obese women have insulin resistance, elevated LH readings are expected. In contrast, we did not discover the same in our research. According to certain research, obese women have a higher gonadotrophin demand for COH due to their gonadotrophin resistant condition.[10] According to some research; obesity has no negative consequences on the ovarian response to IVF. Women in our research groups who were overweight or obese had similar gonadotrophin needs to women who were of normal weight. Also, all three groups received an equal number of days of controlled ovarian hyperstimulation. Some publications have noted poor quality among obese women in terms of oocyte and embryo quality.[14] Some researchers have been unable to connect the two.

Regarding the involvement of the endometrium and the embryo in implantation in obese women, there are still gaps. Several studies show decreased rates of implantation and pregnancy, greater rates of miscarriage, and an increase in problems associated to pregnancy for both the mother and the foetus.[18] Nichols et al. indicate that overweight women undergoing IVF had lower pregnancy rates.[19] Wang et al. agree and support this. Some investigations, however, have come to conflicting results.[20]

Increased rates of miscarriage have been reported in obese women who conceive naturally or following ART. In women with BMIs more than 25 kg/m2, Maheshwari et al. made comparable observations in their systematic study.[10] Regardless of the manner of conception, Metwally et al. also note a comparable tendency in BMI larger than 25 kg/m2.[14] We found no distinction between the three groups in our investigation. The fact that the embryo quality was unaffected by BMI may help to explain this. Abdelmagied AM et. al.[21] came to the same conclusion on BMI and Ovarian stimulation that we did. Ovarian stimulation is significantly influenced by age, AMH, and PCOS status.

Thus, there are no negative impacts of obesity on endometrial thickness, hormone levels, oocyte quantity and quality, implantation rates, or pregnancy rates, according to our study. The function of the endometrium and factors affecting the embryo are still being researched. There are still unknown confounding factors, such as the impact of male obesity on the quality of semen.

The limitations of this study is the sample size, a larger study population would bring about better results. The future work required would be to investigate the molecular interactions between the endometrium and the embryo as well as the impact of male partner obesity on the quality of the semen and, consequently, the quality of the embryo. Comstock et al demonstrated dysregulation of genes encoding cytokines and immune cells during the window of implantation in obese women[22], further research at molecular level would be beneficial. Obesity associated reproductive morbidity is directly proportional to the duration of obesity, hence the obesity in adolescence should be addressed as well.

5. Conclusion

We arrive to the conclusion that an increase in body mass index does not seem to have a negative impact on the success of IVF. Yet, in order to lower pregnancy - related risks, overweight and obese women need to receive weight - loss advice.

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