Impact of maternal Body Mass Index on IVF outcome

Dehat Salah Qadir* Awat Ibrahim Hamadamin** Lava Talat Sharief***

Abstract

Background and objectives: Obesity is a rapidly developing health issue all over the world. Excess body fat causes menstruation abnormalities, particularly chronic oligo-anovulation, as well as infertility. The aim of the current research is to review the impact of women's weight on the outcome of the in vitro fertilization treatment.

Methods: A retrospective single center cohort study was conducted with 129 women undergoing in vitro fertilization cycles from 2022–2023 at Erbil maternity teaching hospital in vitro fertilizaton center. One-hundred-twenty-nine women undergoing assisted reproductive therapy were recruited for the purpose of this study. The target age range of patients was 18-43 years. The study focused on the effect of body mass index on infertility, hormonal status and outcome of in vitro fertilization.

Results: In the normal weight category, there were 18 women (14%), whereas the overweight category comprised 57 individuals (44.1%), and the obese category included 54 participants (41.9%). Primary infertility was observed in 88.9% of the women with normal body mass index, 73.7% and 74.1% of the overweight and obese women respectively. Conversely, secondary infertility was identified in 11.1% of the women with normal body mass index, 26.3% and 25.9% of the overweight and obese women respectively (p>0.05). Regarding pregnancy rates, they stood at 16.7% for the women with normal body mass index, 17.5% for the overweight and 29.6% for obese women (p>0.05).

Conclusion: The findings in our study suggests no relationship between obesity on hormonal levels or clinical pregnancy outcomes

Keywords: Body mass index, Follicular stimulating hormone, In vitro fertilization, Luteinizing hormone

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*M.B.Ch.B, Senior House Officer of Obstetric & Gynecology, KHCMS, Email: dehat1990@gmail.com,.
Corresponding author.
**M.B.Ch.B, FIBMS, MRCOG, Assist. Professor, Consultant in Obstetrics and Gynecology
Email: dr.awat@yahoo.com
***M.B.Ch.B, Msc, MD. Ferility Specialist in Khawar IVF center/Maternity Teaching Hospital. Lecturer in Hawler
Medical University. Email: lavasharief@yahoo.co.uk

Introduction

Obesity is a rapidly developing health issue globally. Excess body fat causes menstruation abnormalities, particularly chronic oligo-anovulation, as well as infertility. Obesity causes hyperinsulinemia and, as a result, ovarian+ hyperandrogenism.[1]According to the most recent data brief from the National Center for Health Statistics (NCHS), women were far more likely than males to have a severe obesity diagnosis (BMI > 30 kg/m2) (11.5%).[2] There is a link between obesity and miscarriage rate and a higher prevalence of pregnancy-induced hypertension and gestational diabetes. Nonetheless, inconsistency of data regarding the influence of obesity on oocyte quality, development of an embryo, the number of mature oocytes, implantation and pregnancy rates in assisted reproduction.[1] In literature, there has been considerable discussion of the negative effects of obesity on ovarian function, and oocyte quality.[3] Obese women undergoing In Vitro fertilization (IVF) have a statistically lower live birth rate (RR = 0.85) than women of normal weight according to a recent meta-analysis.[4] Cytokines have several functions in the ovary during folliculo-genesis and exhibit a complex interaction with inflammation and obesity. Obesity results in lipo-toxicity at the cellular level, which raises the amounts of proinflammatory cytokines in the bloodstream. Target tissues have inflammatory reactions as a result of these cytokines and adipokines. Follicular fluid provides a crucial milieu microenvironment that supports oocyte development while the ovaries are undergoing dynamic tissue remodeling and well-vascularized. Follicular fluid metabolomics are changed in a number of pathways in obese women.[5,6]According to Ruebel et al.'s RNA-seq investigations, obese patients' oocytes exhibit molecular changes. During the analysis of the single-cell transcriptome of germinal vesicle (GV) oocytes from obese patients, a connection was discovered between the expression of the proinflammatory Chemokine C_X_C motif ligand 2 and the levels of blood C-reactive protein (CRP).[7] Additionally, there is mounting evidence that obese people undergoing IVF have reduced endometrial receptivity. functional genomics analysis was utilized by Comstock and colleagues to examine endometrial gene expression patterns in obese women, revealing dysregulation of genes responsible for immune cells and cytokines during the window of implantation.[8] At the organelle level, endoplasmic reticulum stress and mitochondrial dysfunction are linked to obesity.[9,10]The purpose of this study is to review the impact of women's BMI on the outcome of IVF treatment.

Patients and methods

A retrospective cohort study was conducted at a single center with 129 women undergoing In vitro fertilization cycles from 2022–2023 at Erbil maternity teaching hospital_ IVF center. Before the commencement of the IVF cycle or early in the cycle, Consent was taken from the director of IVF center in order to review the files. The target age range of patients was 18-43 years. The inclusion criteria were: 1) women aged between 25-42 years, 2) women who had regular menstrual cycles, 3) women who had at least 3 oocytes harvested, 4) women who underwent Nondonor IVF. Employing a short antagonist regimen, controlled ovarian hyperstimulation was conducted for all subjects. Recombinant FSH and HMG were initiated on either the second or third day of the subsequent cycle, with dosages determined based on various factors including the patient's age, response to prior ovarian stimulation, baseline FSH/LH levels, antral follicle count, and AMH. Adjustments to dosage were made considering serum LH, estradiol levels, and ovarian response on day six of the cycle. Simultaneously, a GnRH

antagonist was introduced to suppress LH; in certain cases, the antagonist's commencement was delayed to the seventh day of the menstrual cycle if follicles were less than 14. Upon the development of at least three follicles reaching a minimum size of 17 mm, subcutaneous hCG injection was administered. Oocyte retrieval occurred 36 hours after hCG administration, followed by embryo transfer on the third day post-oocyte retrieval. A viable oocyte was characterized by a radiant corona, an expanded cumulus, a distinct zona pellucida, an intact first polar body, a translucent cytoplasm, and an absence of debris in the perivitelline area.[11] Fertilization assessment was conducted on the first day following oocyte retrieval, while embryo cleavage was evaluated on the fourth day. On day three, traditional morphological criteria such as cell count and fragmentation were used to assess embryo morphology. A day 3 embryo was defined as having more than eight blastomeres, less than 20% fragmentation, and no multinucleated blastomeres.[12]Data for assessment if BMI were extracted from the patients' medical charts. On presentation the women's height and weight were measured and BMI was calculated for each patient. They were Grouped based on CDC categorization as follows: Normal Weight is defined as BMI: 18.5 to < 25 kg/m^2. [13] Whereas overweight is defined as BMI: 25.0 to <30 kg/m^2, and obese as BMI is 30.0 kg/m^2 or higher. Ethical approval was obtained from the scientific committee of Kurdistan Higher Council of Medical Specialties. The recruited data was analyzed using a statistical program (SPSS, IBM, Chicago) version 25.0. Continuous data were presented using mean and standard deviation, while categorical data were represented as frequencies and percentages. Pearson Chi-square was performed to compare categorical variables among the BMI groups. Regarding BMI groups and continuous variables comparisons, independent t-test was performed. The analysis of variance (ANOVA) was then performed, followed by post-hoc comparisons.

Results

The baseline characteristics of the 129 cases that were included in the study are shown in Table (1). There were 18 women (14%) classified as normal weight, 57 (44.1%) as overweight, and 54 (41.9%) as obese. The mean age of women in the normal weight group was 29.8±4.6 years, in the overweight group was 31.4±6.3 years and 33.2±5.2 years in the obese group was (p>0.05). The average duration of infertility was 8.2±3.8 years among the normal weight group, 6.5±4.3 years among the overweight group, and 9.8±5.1 years among the obese group (p<0.05). Among women of normal weight, 88.9% experienced primary infertility, while for those who were overweight, it was 73.7%, and for those who were obese, it was 74.1%. In terms of secondary infertility, 11.1% of normal-weight women suffered from it, compared to 26.3% of overweight women and 25.9% of obese women. However, there wasn't a statistically significant difference between these groups.

Table (1): Baseline characteristics

Parameters		BMI <25 (n=18)	BMI 25-30 (n=57)	BMI >30 (n=54)	p-value
Age, years±SD		29.8±4.6	31.4±6.3	33.2±5.2	0.064
BMI, kg/m^2		22.84±1.62	27.44±1.31	35.61±4.16	
Duration of infertility, years±SD		8.2±3.8	6.5±4.3	9.8±5.1	0.001
Type of infertility, %	Primary	16 (88.9%)	42 (73.7%)	40 (74.1%)	0.384
	Secondary	2 (11.1%)	15 (26.3%)	14 (25.9%)	
No. of previous IVF trials		0.56±0.5	0.53±1	0.46±0.9	0.898
No. of IUI cycles before IVF		0.4±0.6	0.2±0.5	0.3±0.7	0.331
Continuous variables are shown in mean ± standard deviation (SD). Categorical variables are shown in frequency and percentage					

Table (2) presents the biochemical profiles of the study participants. In the normal BMI group, the mean anti-Müllerian hormone level was 3.11±2.1 ng/ml, while it was 2.7±1.8 ng/ml in the overweight group and 2.9±2.1 ng/ml in the obese group (p=0.634). The mean estradiol (E2) level was 743.4±1137 pg/ml in the normal BMI group, 331.3±598.6 pg/ml in the overweight group, and 511±1017.7 pg/ml in the obese group (p=0.179)). Progesterone (P4) levels were 0.685±0.49 ng/ml in the normal BMi group, 3±16.3 ng/ml in the overweight group, and 4.6±3.6 ng/ml in the obese group (p=0.735). The mean luteinizing hormone (LH) level was 7.8±4.8 IU/ml in the normal BMI group, 4.6±3.6 IU/ml in the overweight group, and 9.3±27.3 IU/ml in the obese group (p=0.39). Follicle-stimulating hormone (FSH) levels were 6.3±2.4 IU/L in the normal BMI group, 9.9±29.1 IU/L in the overweight group, and 11.7±47.35 IU/L in the obese group (p=0.854). The mean prolactin level was 22.2±16.3 ng/ml in the normal BMI group, 26.9±17.3 ng/ml in the overweight group, and 19.3±14.6 ng/ml in the obese group (p=0.052). Thyroid-stimulating hormone (TSH) levels averaged 2.1±1.5 mIU/L in the normal BMI group, 2.5±1.7 mIU/L in the overweight group, and 2.1±1.2 mIU/L in the obese group (p>0.05).

Table (2): Biochemical characteristics

Parameters	BMI <25 (n=18)	BMI 25-30 (n=57)	BMI >30 (n=54)	p-value
AMH level, ng/ml	3.11±2.1	2.7±1.8	2.9±2.1	0.634
E2 level, pg/ml	743.4±1137	331.3±598.6	511±1017.7	0.197
P4 level, ng/ml	0.685±0.49	0.86±0.94	0.84±0.8	0.735
LH level, IU/ml	7.8±4.8	4.6±3.6	9.3±27.3	0.390
FSH level, IU/L	6.3±2.4	9.9±29.1	11.7±47.35	0.854
Prolactin level, ng/ml	22.2±16.3	26.9±17.3	19.3±14.6	0.052
TSH level mIU/L	2.1±1.5	2.5±1.7	2.1±1.2	0.252
P4: Progesterone, AMH: Anti-Mullerian Hormone, TSH: Thyroid Stimulating Hormone, E2: Estradiol, FSH: Follicular Stimulating Hormone, LH: Luteinizing Hormone. Variables are shown in mean ± SD				

Table (3) presents the clinical characteristics and outcomes of in vitro fertilization (IVF) across the three groups. The median number of gonadotropins administered was 24.5 for women who had normal BMI, 28 for the overweight women, and 34.5 for the obese women (p>0.05). Regarding the starting dose, the median was 225 units in the normal weight women and 300 units in both the overweight and obese women (p<0.05). Coasting was implemented in 55.6% of the women with normal BMI, whereas in the overweight group it was implemented in 49.1%, and in the obese group in 59.3% (p>0.05). Follicular stimulating hormone (FSH) alone was utilized for ovulation induction in 50% normal BMI women, 24.6% of the overweight women, and 33.3% of the obese women. Additionally, FSH combined with LH was employed in 50% of those with a normal BMI, 75.4% of the overweight women, and 66.7% of the obese women for ovulation induction. The median time of induction was 8 days for the overweight group and 9 days for both the overweight and obese groups, with statistical significance observed (p=0.08). The median number of retrieved eggs was 8.5 in women who had normal BMI and 7 in both the overweight women and obese women (p=0.336). Furthermore, the median number of fertilized eggs was 4.5 in the women with normal BMI and 5 in the overweight women and obese women (p=0.849). The median number of transferred embryos was 3 in all three groups (p>0.05). In 16.7% of the women who have normal BMI, 17.5% of the overweight women, and 29.6% of the obese women pregnancy was achieved (p=0.255).

Table (3): Clinical characteristics and outcome

Parameters		BMI <25 (n=18)	BMI 25-30 (n=57)	BMI >30 (n=54)	p-value
No. of Gonadotropin used		25.8±7.8 (24.5)	35±26.6 (28)	37.9±16.2 (34.5)	0.105
Starting dose, units		220.8±60.2 (225)	265.4±84.2 (300)	287.5±116.1 (300)	0.041
Coasting (reducing the dose before egg collection)		10 (55.6%)	28 (49.1%)	32 (59.3%)	0.559
Hormone used	FSH alone	9 (50%)	14 (24.6%)	18 (33.3%)	0.123
	FSH+LH	9 (50%)	43 (75.4%)	36 (66.7%)	
Total No. of days needed for stimulation		8.4±0.98 (8)	8.8±1.4 (9)	9.5±1.7 (9)	0.008
No. of collected eggs		8.94±5.4 (8.5)	7.3±5.1 (7)	8.96±7.7 (7)	0.336
No. of fertilized eggs		5.8±4 (4.5)	5.5±4.1 (5)	5.9±3.8 (5)	0.849
No. of transferred eggs		3±1 (3)	2.5±1.1 (3)	2.8±1.13 (3)	0.120
Clinical Pregnancy	Yes	3 (16.7%)	10 (17.5%)	16 (29.6%)	0.255
	No	15 (83.3%)	47 (82.5%)	38 (70.4%)	
Continuous variables are shown in mean ± standard deviation (Median). Categorical variables are shown in frequency and percentage					

Discussion

In overweight and obese women, the primary reason for difficulty in conceiving has been found to be the absence of ovulation.[13] Studies have reported Lower conception rates in normal menstruating obese women such that there is 5% decreased chance per unit rise in BMI beyond 29 kg/m2. There are controversial opinions regarding effects of BMI on regulated ovarian stimulation in obese women.[14-18] In terms of duration of infertility, we found a significant association between the duration of infertility and BMI. We noticed that women whose BMI exceeds 30 experienced a notably longer period of infertility in comparison to those with a lower BMI. Sathya et al. also found similar results and their finding was also statistically insignificant.[1] In our study, the percentage of primary infertility was higher among all three groups, compared to secondary infertility. However, when comparing between the three groups we observed a higher percentage of primary infertility among women with normal BMI (88.9%), compared to women with higher BMI (73%, 74% respectively). This can be due to uterine anomalies or male factors, for example semen abnormalities.[19,20] Both conditions are important causes of infertility. Moreover, a higher percentage of secondary infertility was reported in overweight and obese women (26%, 25.9% respectively) compared to those of normal weight (11%). This can be linked to junk food ingestion, and sedentary lifestyle. Dhandapani et al. observed a higher percentage of women with normal BMI in those with primary infertility compared to secondary infertility.[21] Anti-Mullerian Hormone (AMH) serves as one of the most potent indicators for the quantity of oocytes obtained in a COH-IVF cycle. Although statistically insignificant, we found that AMH level was higher in women with normal BMI than those with higher BMI. This finding is in accordance with Buyuk et al.'s study in which they reported that AMH of women with increased BMI is significantly lower than those with normal BMI.[22] In our study, we found that women whose BMI is normal tend to have higher levels of estradiol (E2) in comparison to those whose BMI is higher. Thomas et al.'s study yielded similar findings, indicating that serum estradiol (E2) levels were notably lower in women who have higher BMI compared to those who have normal BMI.[23] Shen et al. also reported higher serum E2 levels in women with normal BMI compared to women with higher BMI.[24] Obese women are more liable to have elevated LH readings.[25] However, in the current study we found no significant association between LH and BMI. This finding is also similar to Sathya et al., and Liu et al.'s studies in which they reported no significant correlation between LH and BMI.[1,26] Moreover, in our study FSH was higher among overweight and obese women, however this finding was not statistically significant. This in accordance to Sathya et al.'s finding [1] but in contrast to Liu et al.'s study in which higher levels of FSH was significantly associated with normal weight women when compared to higher BMI groups. [26] In contrast, Shen et al found significantly higher FSH levels among women who have normal BMI compared to those who have higher BMI.[24] In this study the starting dose of gonadotropin was considerably higher in the overweight and obese women compared to women with a normal BMI. Similarly, Shen and colleagues discovered that women who have a higher BMI received a significantly higher dose of gonadotropin in comparison to those who have a normal BMI.[24] Moreover, our investigation revealed that induction in obese and overweight women necessitate a longer duration in comparison to women who are of normal weight. Similarly, Shen et al. noted that the induction period in women with higher BMI was notably longer than in

women with normal BMI.[24]In the present study we found that BMI has no role in the outcome of IVF. This finding is in accordance to Sathya et al.'s study in which they found no significant association between BMI and IVF outcome.[1] Nicholas et al. and Wang et al. and Rittenberg et al. all concluded a reduced conception rates in the overweight group undergoing IVF trials.[27-29] In our study, we noticed that overweight and obese women had a slightly higher chance of conception compared to women of normal weight. However, this difference wasn't strong enough to be considered statistically meaningful, therefore it might be a coincidence. This can be attributed to the higher prevalence of primary infertility in the normal weight group and the higher prevalence of secondary infertility in the overweight and obese groups, found in our study. This finding is in accordance to Liu et al.'s finding in which they found no significant association between clinical pregnancy and BMI groups. [26]

Conclusion

Our study findings do not suggest adverse effects of obesity on hormone levels or clinical pregnancy rates. However, number of gonadotropins use and the starting dose that is administered for ovarian stimulation is affected by higher BMI.

Conflict of interest

The authors declare no conflict of interest.

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