ORIGINAL ARTICLE

Effect of Body Mass Index on the Outcome of In-vitro Fertilization/Intracytoplasmic Sperm Injection

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ABSTRACT

Background and Objective: Obesity is becoming a global issue related to many health problems, and infertility is one of them. It has been established in literature that obesity or increased body mass index (BMI) harms the ability of a woman to conceive. Assisted reproductive techniques e.g., in-vitro fertilization (IVF) and Intracytoplasmic Sperm Injection (ICSI) are helping infertile women to conceive. This study's objective was to analyze the effect of BMI on IVF/ICSI treatment outcomes in infertile women.

Methods: This was a retrospective cross-sectional study. Samples of 500 patients aged less than 40 years were selected at a tertiary care infertility center: Lahore Institute of Fertility and Endocrinology, Hameed Latif Hospital. The sample was collected from January 2019 to June 2019. A structured proforma was used to collect information about selected anthropometric measurements and ultrasonography findings from the files and follow-ups of the selected patients. Data was processed and analyzed in Statistical Package for Social Sciences (SPSS) version 20.0.

Results: The age of the subjects ranged from 18 to 39 years, with a maximum number of subjects in the age category 31 to 35 years. BMI was significantly associated with number of follicles retrieved and clinical pregnancy rate (P = 0.001).

Conclusion: Normal BMI has positive impact both on follicular response in controlled ovarian stimulation (COS) and clinical pregnancy rates in women undergoing IVF/ICSI treatment.

KEYWORDS: Body Mass Index, Pregnancy Rate, Obesity, Intracytoplasmic Sperm Injection.

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INTRODUCTION

Obesity has become a global issue and is believed to be associated with wide-ranging health complications, including heart disease and cancer. To what extent obesity affects fertility and causes complications in pregnancy is a matter of concern for infertility specialists and researchers.

High BMI adversely affects reproductive outcomes significantly. Despite its effect on the possibility of getting pregnant, it also has a detrimental impact on the health and outcome of the resulting pregnancy.[1] The harmful effects of obesity on general health are well known, and these include menstrual disorders, infertility and maternal complications in pregnancy.[2]

The prevalence of obesity is rising to epidemic proportions at an alarming rate in 'westernized' and in less developed countries, especially in urban areas. The health, economic and psychosocial consequences of the increasing incidence of obesity is substantial.[3] Obesity also potentially adversely affects the endometrial lining, implantation, and early fetal development.[4]

Obesity not only disturbs fertility but also poses difficulties in treating such patients. It has been postulated that obesity negatively impacts fertility through an effect upon the control of ovulation, egg development, embryo development, endometrial maturity, conception and pregnancy loss.[5]

Assisted reproductive techniques (ART) are the treatments offered to patients with blocked tubes or sperm deficiencies where fertilization/embryo formation cannot take place inside the womb. Hence, the fertilization occurs in the laboratory, and the resulting embryos are transferred back in the womb after two to four days, where implantation/conception takes place in the same manner as natural pregnancy.

There are many centers in the world offering this technique to the infertile couples. But even in best centers, the success rate is 30 – 40%. This low rate could be due to some deficiency in the techniques or natural protection against abnormal eggs and sperms. However, in women undergoing infertility treatments, the effects of obesity on number of ovarian follicles egg quality, embryo quality, clinical pregnancy; live birth rates are controversial.[6,7]

In this study, the authors were interested in determining the effects of BMI i.e., how obese and non-obese patients differ in their ovarian response and pregnancy outcome by ART. Treatment protocols are made at the clinic level, and the variation in clinic policy regarding fertility treatment for obese women is not readily available, raising questions whether access to fertility-related services is conditional on body mass index.[8]

METHODS

It was a retrospective cross-sectional study approved by Ethical Review Board vide Letter No. (LIFE 07-10-2019)**.** All infertile women (who did not conceive naturally within 1 year after marriage) coming to Lahore Institute of Fertility and Endocrinology (LIFE) for ART treatments from January 2019 to June 2019, women age less than 40 years and with the regular menstrual cycle were included. Women above 40 years of age and with hormonal abnormalities and past history of ovarian surgery were excluded from the study. Non-probability convenient sampling technique was used. The sample size was calculated through World Health Organization statistical software "S. Size". The total estimated sample size was 500, which was sufficient to detect the difference of 10% outcome between obese and non-obese at significance level (α = 5) with the power of the study (1-β) = 80%. The BMI was calculated from the formula (weight in kg/height in meter^2).[9]

These women were stimulated with the same protocol, the primary outcome measure being the total number of follicles in both ovaries on the day of the decision of egg retrieval. According to the number of follicles, the response of ovaries was arbitrarily classified into good, average, and poor. Less than 5 eggs were considered a poor response. 5 – 9 eggs retrieval was regarded as an average response, while more than 10 eggs retrieved were deemed to be the good ovarian response.These patients were followed for their clinical pregnancy outcomes. The selected women were given COS with long agonist protocol. Initially, down-regulated with GnRH agonist from the mid-luteal phase of the menstrual cycle followed by stimulation with recombinant FSH on day 2/3 of the subsequent cycle. HcG was administered subcutaneously when at least 3 follicles were $\geq$ 18 mm in diameter or above. It was followed by ovum pick-up and embryos.

STATISTICAL ANALYSIS

The data was entered in Statistical Package for Social Sciences (SPSS) version 20. For continuous variable, mean and standard deviation was calculated while for categorical variables frequencies and percentage was calculated. Pearson Chi-Square was used to compare the statistical difference between the different variables. The level of significance was 5%.

RESULTS

The quantitative data showing frequency and percentage of age category of 500 subjects revealed

that they were 8 subjects in less than 20 years category. In the age category of 21-25 there were 89 subjects (17.8%). In the age group of 26-30 years, there were 172 subjects (34.4%). There were 184 subjects (36.8%) in the age group of 31-35 years, while in the age group of 36 and above, there were 47 subjects (9.4%).

This shows that there were maximum numbers of subjects in the age group of 31-35 seeking IVF/ ICSI treatment.

Figure:1 revealed that out of 500 subjects, 57 (11.4%) showed inadequate ovarian response while the average response was seen 113 subjects (22.6%). 330 items (66%) showed a good response.

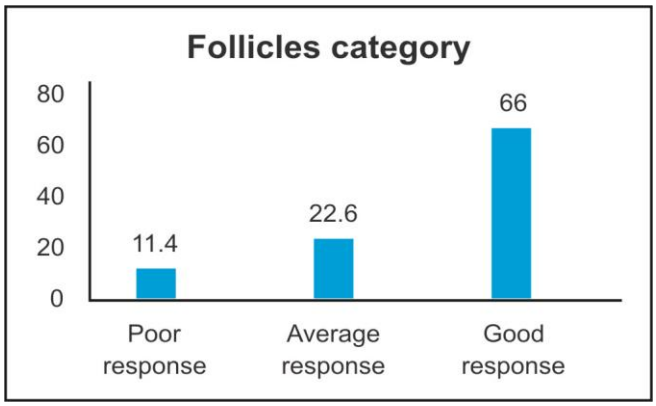

Fig.1: Percentage of Ovarian Response.

According to results, 183 (36.6%) subjects had a normal BMI, 180 subjects (36%) were overweight while 91 (18.2%) were in the category of obese and 46 (9.2%) fell into the morbidly obese category. Maximum number of 183 subjects was from the standard BMI category while morbidly obese category had minimum number of 46. When data were analyzed for the pregnancy outcome of 500 subjects 331 (66.2%) had negative pregnancy outcomes and 169 (33.8%) had positive pregnancy outcomes.

Association of BMI categories with pregnancy outcome was analyzed, showing that there were 88 negative and 95 positive pregnancies in the standard in BMI category, while in the overweight category, 113 were negative while 67 were positive. Out of 91 obese patients, 86 had negative pregnancy tests, while only 5 had positive outcome. Only 2 positive pregnancies were seen in 46 morbidly obese patients. This association was significant (P=0.001) (Table-1).

Association of BMI categories with the follicular ovarian response showed that out of 183 subjects of standard weight, only 6 had poor response; the average response was 24, while 153 subjects had good ovarian response. In the overweight category, there were 180 subjects of whom 9 had a poor response, 39 had an average response, and 132 subjects had a good response. In the obese category, the total number was 91 subjects, of whom 16 had poor response, 34 had an average response, and 41 had a good response. In the morbidly obese category, the total number of subjects was 46, of which 26 had a poor response, 16 had an average response, and only 4 had a good response (Table-2).

According to the association of mean BMI with pregnancy outcome, 331 subjects with a mean BMI of 28.47 showed negative pregnancy outcomes, while 169 subjects with a mean BMI of 24.75 had positive pregnancy results (P = 0.001) showing low BMI having a positive impact on pregnancy outcome.

Table-1: Association of BMI categories with pregnancy outcome.

Variables	*Body Mass Index*					
Outcome	*Normal*	*Overweight*	*Obese*	*Morbidly Obese*	*Total*	*p-value*
Negative pregnancy	88	113	86	44	331	
Positive pregnancy	95	67	8	2	169	0.001
Total	183	180	91	46	500	

Table-2: Association of BMI categories with ovarian response.

Follicular	*Body Mass Index*					
Response	*Normal*	*Overweight*	*Obese*	*Morbidly Obese*	*Total*	*p-value*
Poor	6	9	16	26	57	
Average	24	39	34	16	113	0.001
Good	153	132	41	4	330	
Total	183	180	91	46	500	

DISCUSSION

The present study investigated the effect of body mass index on the treatment outcome of infertile women undergoing ART. Different BMI categories were compared for the number of follicles seen on decision day, the number of eggs retrieved on egg pick-up day, and a positive pregnancy test.

Women having higher BMI values were found to have a lower number of follicles, a lesser number of eggs, and have a smaller number of positive pregnancy tests.

The mean BMI of patients with positive pregnancy outcome was calculated, it fell in the normal weight category according to WHO cut-off values. While the mean BMI of patients with negative pregnancy outcomes fell within the overweight group. This shows that women with high BMI have lower chances of becoming pregnant than women of normal BMI.

Deleterious effects of high BMI on IVF outcome are being documented by different studies.[10,11] Weight loss results in significant improvement in pregnancy and ovulation rates in anovulatory obese women.[12] A study investigating the effect of BMI on IVF outcome, review, and meta-analysis showed that women who are overweight or obese (BMI ⩾ 25 kg/m^2) tend to have a poorer pregnancy rate following IVF treatment than women with normal BMI.[13] Another meta-analysis clearly demonstrates that raised BMI is associated with a significantly reduced live-birth rate and increased miscarriage rate after IVF treatment.[14]

The present study analysis of the association of BMI categories with pregnancy outcome (Table-2) showed that in the standard BMI category, there were 95 positive pregnancies (51%), while in the overweight category, 67 were positive (37%). In obese patients, only 8 had a positive outcome (8%). Only 2 positive pregnancies (4%) were seen in morbidly obese patients. This association was checked with the Chi-Square showing significant association with a P-value of 0.001.

Another case–control study observed that women with a BMI > 25kg/m^2 had poorer implantation and pregnancy rates with increased chances of miscarriage.[15]

Renowned gynecologists and reproductive health specialist have observed the reproductive health issues in populations with increasing weight as a higher frequency of women diagnosed with disorders of menstruation, infertility, and diabetes mellitus in pregnancy and other related complications.[2]

Many studies have been carried out to see the effect of weight reduction in improving reproductive function in overweight and obese infertile women. There is now a better understanding of how weight reduction through dieting/exercising can lead to improved reproductive outcomes.[16,17]

The British Fertility Society has formulated policy and practice guidelines directing clinicians to advise their patients to try to lose weight to normal BMI preceding fertility treatment.[18] In the present study, a negative association was seen between high BMI category and follicular ovarian response.

Similar results were demonstrated in a study where detrimental effects of high BMI on the quality and maturity of follicles and eggs were observed, concluding that increased body mass index (BMI) is linked with ovulatory sub-fertility and anovulatory infertility.[19] Overweight and obese women have poorer pregnancy outcomes following fertility treatment.[20, 15] They respond to clomiphene induction of ovulation is poorer and need higher doses of gonadotropins for ovarian stimulation,[21] resulting in fewer follicles and harvesting less number of oocytes. In-vitro fertilization rates are reduced, and the embryo quality is also marginalized in obese.[22]

In some studies, the pregnancy rate is lower, and there is an increased risk of early pregnancy loss.[23] Weight loss can help regularize menstrual cycles and increase the chance of spontaneous ovulation and conception in obese women with anovulatory menstrual cycles.[24,25]

CONCLUSION

The high body mass index has a negative effect on ART treatment outcome i.e., ovarian response and clinical pregnancy. To achieve an optimal response to treatment, women must be encouraged to gain normal BMI before start of therapy.

LIMITATIONS OF THE STUDY

This study was done in one department of the hospital so the sample size was small. The results

may be more precise and accurate if study will be based on a multicentre approach with a larger sample size.

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CONFLICT OF INTEREST

None to declare

GRANT SUPPORT & FINANCIAL DISCLOSURE

None to disclose.

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Author's Contribution

ZI: Conception, study design, data collection.

HLK: Compilation, and drafting of manuscript.

RN: Drafting and reviewing the manuscript.

HH: Data collection.

RN: Acquisition of data, data analysis and interpretation.

ALL AUTHORS: Approval of the final version of the manuscript to be published.