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Research Article

Effect of Body Mass Index on Pregnancy Outcome in in Vetro Fertilization, Retrospective Observational Study

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Abstract

The prevalence of obesity has increased dramatically over the past few decades, it is associated with infertility in females by multiple methods. As a result, it is important to look at the effect of rising BMI on the IVF outcomes.

Our study was a retrospective analysis of outcomes from IVF of 2633 women. to determine the effect of female age and BMI on success of IVF cycle, pregnancy rate, number of oocytes retrieved, number of mature eggs and live birth over a period of 6 years from 2010-2016.

It showed that the success rate of pregnancy and live birth decrease with increasing maternal age. There is significant inverse correlation between female age and total oocyte retrieved with Pearson Correlation p-value 0.001, and inverse correlation between female age and number of mature eggs. Success rate of IVF most favorable in patients with younger age and normal BMI which was addressed by other studies.

Around the world fertility treatment is withheld from women above a certain BMI, so ethical considerations should be looked, and individualization of each case before applying the rules of offering or not of IVF treatments and we must weigh the risks and benefits in deciding whether to restrict access to IVF for those with elevated BMIs.

Keywords: *IVF Treatment; Infertility; Ethical Considerations*

Abbreviations

BMI: Body Mass Index: IVF: In Vetro Fertilization; SD: Standard Deviation

Introduction

The prevalence of obesity has increased dramatically over the past few decades , In the United States alone, almost two thirds of women are obese [4], In State of Qatar, More than 70 percent of the population is either overweight or obese [15].

Obesity is associated of range of consequences which can impair reproduction as it can cause menstrual cycle abnormalities, impairs ovarian responsiveness to gonadotropin stimulation during ovulation induction and decreased oocytes retrieved [4], obesity and overweight are significantly associated with decreased pregnancy rates, increased requirements for gonadotrophins and higher miscarriage events, high BMI is also associated with adverse pregnancy outcomes such as gestational diabetes, hypertension and premature labor [18].

Definition of obesity: It's a disease of excess body fat that is strongly associated with insulin resistance. Categories of adult obesity are based upon body mass index (BMI) (Table a).

On a population basis, BMI positively correlates with percent body fat, although this relationship varies among individuals by sex, age, and race-ethnicity, beside the health problems and conditions that are associated with obesity mentioned previously, obesity can impair reproduction in both women and men, leading to infertility in couples trying to conceive, subsequent complications in pregnancy, and adverse effects on their offspring.

Category	BMI (kg\m^2)
underweight	<18.5
Normal	18.5-24.9
Overweight	25-29.9
Obesity, grade I	30-34.9
Obesity, grade II	35-39.9
Obesity, grade III	≥40

Table a: *Category of obesity by BMI (body mass index WHO 2004).*

The factors that contribute to infertility in women are explained by multiple changes:

- Menstrual cycle abnormalities: excess weight and abdominal fat increase the risk of having menstrual abnormalities [7,10].
- Ovulatory dysfunction: Obesity is commonly associated with ovulatory dysfunction. Obese women with a BMI >27 kg/m^2 have a relative risk (RR) of anovulatory infertility of 3.1 (95% CI, 2.2- 4.4) compared with their lean counterparts with a BMI 20.0-24.9 kg/m^2 [9,16].
- Altered ovarian responsiveness and oocycte quality, multiple studies confirm that obesity impairs ovarian responsiveness to gonadotropin stimulation (i.e., increased duration, amount of gonadotropin administered, cycle cancellation; decreased oocytes retrieved) [8,17].

Another important factor determine fertility is age, fertility declines as a woman ages due to the normal age-related decrease in the number of eggs that remain in her ovaries [3,13]. Although fertility declines for both men and women as they age, this happens much more sharply for women. Women not only have fewer eggs as they get older, the quality of the remaining eggs also declines (RCOG).

Objective

To determine the effect of female age and BMI on success of IVF cycle, pregnancy rate, number of oocytes retrieved, number of mature eggs and live birth.

Design

Retrospective analysis of outcomes from IVF treatment during a period from 2010-2016.

Materials and Methods

Study design and study area

It is a retrospective study, conducted in Assisted Reproduction Department, Women's Hospital, currently known as Women's Wellness and Research Center, Hamad Medical Corporation, Doha, Qatar. it is a governmental hospital and the largest women's tertiary hospital in the country with average deliveries of 17,000 births per year. it has 7 operating theatres and 26 delivery rooms.

Study sample

Design

- Retrospective study involved 2633 had IVF (*in vitro* fertilization) treatment.
- The study sample included women who had IVF in our facility who had antenatal care and gave birth in the hospital in the period from 2010-2016.
- The data were collected from the maternal records for analysis and was kept in a password-protected Excel sheet (© 2010 Microsoft Corporation).

Data extraction

The records included information on subjects' demographics age, BMI, out come if women got pregnant or not, total oocyte retrieved, fertilization rate, blastocyst rate, maturation rate and live birth.

Statistical analysis

- Descriptive analysis of mean ± standard deviation (SD), median, minimum and maximum for continuous variables were performed using SPSS version 20.0.
- Comparisons were done using T-test, ANOVA, and chi-square test.
- 95% CI was used to assess the statistical significance of association among variables, with a P value less than 0.05 was used as a cut-off point to see the presence of a statistically significant association.

Ethical considerations

Ethical clearance for the study was obtained from the Medical Research Center, (MRC), Hamad Medical Corporation (HMC), Doha- Qatar, Ref No: 16427/16. To protect the patient confidentiality, the identifiable information as name of the patients and health number was excluded from the extracted data and replaced with specific code generated for the study

Results

		Female Age:	Patient BMI	Total Oocyte Retrieved	# of Mature eggs
N	Valid	2633	2633	2633	2633
Mean		30.90	31.1970	13.98	10.40
Median		31.00	30.8000	13.00	10.00
Std. Deviation		4.551	6.28170	7.317	5.920
Percentiles	25	28.00	27.0600	8.00	6.00
	75	34.00	34.7000	18.00	14.00

Table 1: *Mean and SD of variables.*

Age and BMI in pregnancy:

- Mean age in the pregnancy group 30.60 ± 4.38 , and in no pregnancy group was 31.1 ± 4.68
- Mean BMI in pregnant group 31.14 ± 6.31 , and in no pregnancy group 31.25 ± 6.25.
- Using t-test age is significantly lower in the pregnancy group compared with no pregnancy with a p-value 0.001 CI (0.23 - 0.93); the magnitude is less than 1 year, There is no huge differences in the means but due to big number of data it came to be significant different , on the other hand, BMI is same in both the groups with a p-value 0.663 CI (-0.37 - 0.58).
- Live birth is significantly lower with higher female age with P-value of 0.001 CI (0.52 - 1.38).

		Total Oocyte Retrieved	number of Mature eggs
Female Age:	Pearson Correlation	-.224**	-.186**
	Sig. (2-tailed)	0.001	0.001
Patient BMI	Pearson Correlation	-0.035	-0.018
	Sig. (2-tailed)	0.075	0.358

Table 2: *Pearson Correlation between female age and BMI to total oocyte retrieved and number of mature eggs.*

- There is significant inverse correlation between female age and total oocyte retrieved with Pearson Correlation p-value 0.001.
- And inverse correlation between female age and number of mature eggs with p-value 0.001.
- There is an inverse correlation between BMI and total oocyte retrieved and number of mature eggs, but p-value is non-significant.
- We went a step further with the present study by looking at subgrouping the population with the goal of isolating types of obesity and to look for the effect of each subgroup on total oocyte retrieved, maturation rate, fertilization rate, blastocyst rate, rate of pregnancy and live birth.

After classification of BMI to subgroups

		Mean	SD
Total Oocyte Retrieved	Under weight	12.8	5.62
	Normal weight	13.8	6.74
	Pre obese	14.6	7.69
	Class I	18.8	7.40
	Class II	14.0	7.32
	Class III	12.9	6.40
	Total	13.9	7.31
Maturation rate	Under weight	78.5	15.49
	Normal weight	75.74	20.50
	Pre obese	76.38	19.48
	Class I	75.05	19.30
	Class II	76.90	18.03
	Class III	72.75	21.64
	Total	75.49	19.50

Blastocyst rate	Under weight	12.08	18.36
	Normal weight	6.25	14.36
	Pre obese	10.59	21.51
	Class I	8.28	18.77
	Class II	8.60	19.81
	Class III	4.44	11.61
	Total	8.33	18.66
Fertilization rate	Under weight	80.47	16.92
	Normal weight	78.52	57.07
	Pre obese	70.71	22.70
	Class I	74.18	42.14
	Class II	71.05	50.08
	Class III	88.96	114.83
	Total	74.56	47.58
pregnancy	Under weight	0.13	0.35
	Normal weight	0.078	0.26
	Pre obese	0.05	0.23
	Class I	0.071	0.25
	Class II	0.081	0.27
	Class III	0.037	0.19
	Total	0.070	0.25
Live birth	Under weight	0.25	0.44
	Normal weight	0.32	0.46
	Pre obese	0.36	0.48
	Class I	0.31	0.46
	Class II	0.29	0.45
	Class III	0.32	0.47
	Total	0.32	0.46

Table 3: *Classification of BMI groups and the distribution female age, total oocyte retrieved, maturation rate, fertilization rate, blastocyst rate, rate of pregnancy and live birth.*

- Using ANOVA, shows increasing female age led to increase BMI with P-value 0.001 CI (30.72 - 31.07)
- There is significant lower fertilization rate with increase BMI with P-value of 0.004 CI (72.76 - 76.38) And Blastocyst rate with P-value 0.003 CI (7.61 - 9.05)
- There is no significant difference maturation rate, pregnancy rate and live birth with change of BMI.

Discussion

As our population getting obese, it is important to look at the effect of rising BMI on the IVF outcomes.

The present study representing the largest study done in Qatar. It showed that the success rate of pregnancy and live birth decrease with increasing maternal age which is approved by other studies [3,6,13].

In addition success rate of IVF most favorable in patients with normal BMI which was addressed by other studies [14]. Race can play an important role in classification of BMI as in 2004 the WHO recommended lowering the BMI cut-offs for Asian adults for overweight from 25 to 23 kg/m^2 and for obesity from 30 to 27.5 kg/m^2 [19]. Also India has adopted the lower BMI cut-off points of 23 kg/m^2 for overweight and 25 kg/m^2 for obesity [1].

In our study we followed the international WHO classification of BMI without looking to the patients race which may alter the result given the fact that we didn't standardize the race of our patients.

Increase BMI has a significant impact on embryo quality as measured by blastocyst formation. This result was similar to other studies [11] who concluded that the blastocyst formation rate was significantly better in the normal-weight controls versus overweight/obese patients. We can conclude from both studies that maternal BMI has a significant impact on embryo quality as measured by blastocyst formation. A decreased blastocyst formation rate can lead to poorer reproductive outcomes in overweight and obese women with infertility [11].

There was decrease in fertilization rate and blastocyst rate , this finding was agreed by other studies [5] but different from a study by [2] who concluded no difference in fertilization rate or blastocyst rate in obese women compared with normal BMI However, implantation, pregnancy, and live birth rates were poorer in obese women [2].

Around the world fertility treatment is withheld from women above a certain BMI, with a threshold ranging from 25 to 40 kg/m^2. Arguments for a BMI cutoff cite: First, lower success rates of fertility treatment in overweight and obese women. Second, increase obstetric and perinatal complications. Third, increase cost of fertility treatments. On the other hand, the ethical principles play here are autonomy, nonmaleficence, proportionality and beneficence.

Autonomy: allowing or enabling patients to make their own decisions about which health care interventions they will or will not receive [11]. Nonmaleficence: principal of not inflicting harm on others. Proportionality: weighing and balancing individual freedom against wider social goods. Beneficence, the principle of beneficence is a moral obligation to act for the benefit of others. There are 2 aspects of beneficence: providing benefits and balancing benefits of risk or harm. The principle of justice obliges us to equitably distribute benefits, risks, costs, and resources. The following arguments (rules) are supported by the principle of justice: To each person an equal share and according to the need [12].

In summary: one must weigh the risks and benefits in deciding whether to restrict access to IVF for those with elevated BMI or not.

The arguments against weight restriction favor patient autonomy as the guiding principle. IVF risk is perceived, weight loss is hard, often not successful and the impact of age is significant.

The arguments for restriction favor non-maleficience, it can be argued it is unethical to subject a patient to lower IVF success rates and increased obstetric and perinatal complications.

NICE guidelines suggest that women should be informed that BMI should ideally be in the range 19-30 before commencing assisted reproduction, and that a female BMI outside this range is likely to reduce the success of assisted reproduction procedures.

One can conclude that it is ethically justifiable to have BMI restrictions for access to IVF treatments, but there will be debate about which BMI cut point to use for our population in Qatar considering the high percentage of obesity. Currently we used BMI of 35 as a cuff-off in our department.

Funding for fertility treatment service in Qatar limited under criteria of specific age and BMI and therefore, strict guidance exists regarding who can be offered treatment.

There are number of limitations of this study, first, only female BMI could be analyzed because male BMI was not recorded. Second, we were unable to adjust for patient race among BMI categories, because although race is included in the patient's files, we unfortunately did not have that information in our data collection database, Earlier studies have seen an interaction between race and BMI, suggesting that this may be a true limitation, finally, other risk factors were not collected for study which may influence the success of the IVF.

The major strength of our study is that the women were seen in a tertiary center, which helped to obtain the data from one source.

Conclusion

A woman's age must be considered as a prognostic factor when IVF is proposed to infertile couples.

Ethical considerations should be looked, and individualization of each case before applying the rules of offering or not of IVF treatments and we must weigh the risks and benefits in deciding whether to restrict access to IVF for those with elevated BMIs.

Competing Interest

The authors have no financial or non-financial interests to declare in relation to this article.

Contribution to Authorship

All authors contributed in planning and conducting the study, SE and applied for the approval, HB collected the data ,data analysis done by SE , MST. TM, MA contributed in the interpretation of the data, SE and MST wrote the first draft, and revision done by all authors.

All authors approved the final version for submission.

Ethical Approval

The research related to human use has been compiled with all relevant national regulations. Institutional policies and in accordance with the tenets of the Helsinki declaration. The study has been approved by the local institutional review board at Medical research center (MRC), Hamad Medical Corporation, Doha- Qatar, reference No: 16427/16. Informed consent was waived due to the retrospective design of the study.

To protect the patient confidentiality, the identifiable information as name of the patients and health number was excluded from the extracted data and replaced with specific code generated for the study.

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Availability of Data and Materials

The data of the current study are available from the corresponding author on reasonable request.

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