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Impact of Age on Ovarian Response and IVF Outcome during Controlled Ovarian Hyperstimulation in Women from Gaza Strip

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Abstract

***Background**: Although age is an important factor in female fertility, not much date were focused on the relationship between age and ovarian response and in vitro fertilization (IVF) outcome. However, the female reproductive capacity varies with age.*

***Objective:** To assess the impact of age on ovarian response and IVF outcome during controlled ovarian hyperstimulation in women from Gaza Strip.*

***Methods:** This prospective cohort study consisted of 75 women attending IVF at Al-Basma Fertility Center in Gaza City. The number of oocytes and embryos were recorded for each female and the occurrence of pregnancy was followed for three months. The obtained data were computer analyzed using SPSS statistical package version 18.*

***Results:** The mean age of the study population was 29.2±5.9 years. The total number of oocytes was significantly decreased with increasing age (F=3.932 and P=0.024).In this context Pearson correlation test exhibited negative significant correlation between women age and the number of mature oocyte (r=-0.276, P=0.017). There was an inverse relationship between age and ovarian response (F=6.773 and P=0.001), showing good response (9-16 oocytes) at mean age of 26.7±5.0 years. When related to women age, IVF outcome showed that the chance of getting pregnant increased with decreased age (F=4.278 and p= 0.018).*

***Conclusion:** The ovarian response and the chance of getting pregnancy were diminishing with ageing, implying that maternal age should by consider during IVF program.*

***Keywords:** Female age, Ovarian response, In vitro fertilization outcome, Gaza Strip.*

Introduction

Controlled ovarian hyperstimulation (COH) refers to a regime of fertility medication that used to stimulate the development of multiple follicles of the ovaries in one single cycle, resulting in superovulation. Controlled ovarian hyperstimulation for *in vitro* fertilization (IVF) cycles is usually monitored by serum estradiol levels and pelvic ultrasonography with two purposes: (1) to obtain an adequate number of mature oocytes, and (2) to prevent the risk of severe ovarian hyperstimulation syndrome.[1,2] However, maternal age is of a particular concern prior to COH in the general practice of IVF treatment.[3,4]

Female age is the single most important determinant of spontaneous as well as treatment-related conception, with a gradual decline in fertility especially after the age of 35 years.[5,6,7,8] A putative cause of such decline in fertility was attributed to diminished ovarian reserve which refers to the number and quality of oocytes.[9] Older women may be more likely to be diagnosed with unexplained infertility and that this is due to the negative effect of age on ovarian reserve.[10] Nonetheless, the relationship between age and declining reproductive capacity is highly variable.[11,12]

Although extensive research has been carried out globally on IVF to achieve pregnancy,[3,8,9] just recently two studies have been conducted in Gaza Strip and published in this regard entitled "Anti-mullerian hormone as a predictor of ovarian reserve and ovarian response in IVF women from Gaza strip"[13] and "Serum estradiol level as a predictor of ovarian response and pregnancy outcome during controlled ovarian hyperstimulation in women from Gaza Strip".[14] However, there was no previous studies related age to COH or even to the IVF outcome. Therefore, the present study is the first one to assess the impact of age on ovarian response and IVF outcome during COH in women from Gaza Strip.

Methods

This prospective cohort study consisted of 75 women undergoing COH program and aged between 20-40 years without history of other diseases. The subjects were recruited

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from Al-Basma fertility Center in Gaza City in the period September 2011 to November 2011. Each patient gave informed consent to participate in the study. The criteria for inclusion were as follows: (i) age 20–40 years, (ii) regular menstrual cycle, (iii) not on hormone therapy for three months and (iv) have not been subject to surgical operation in the reproductive system. This study was approved by the Ethical Committee of the institution. All participants were guaranteed confidentiality, and only the principal investigator has full access to the data.

In Vitro Fertilization Protocol

There were two protocols used during ovarian hyperstimulation, the first one is long protocol, which relies on pre-stimulation pituitary down regulation using GnRH agonists in daily intermittent or depot formulations. The second one is short protocols using GnRH antagonist during the late follicular phase of the stimulation cycle have been utilized. Adding recombinant LH to recombinant FSH protocols, when starting antagonists, as a strategy to increase oocyte yield and improve pregnancy rates. Human chorionic gonadotropin (hCG) was injected at a dose of 5000 or 10,000 IU. Oocyte retrieval for IVF was then typically scheduled for 30–34 hr thereafter. Then the fertilized oocyte was placed in G1 media for 3-4 days then in G2 media before rewind. The vaginal sonography was performed in the second day of the menstrual cycle to assess the extent of the responsiveness of the ovary. The number of oocytes and embryos were recorded for each female and the occurrence of pregnancy was followed for three months.

Statistical analyses

Simple distributions of the study variables and cross tabulation were applied. One-way ANOVA test was used for evaluating the relation between age and qualitative and quantitative variables. Pearson correlation test was applied. The results in all the above mentioned procedures were accepted as statistically significant when the p-value was less than 5% ($p<0.05$).

Results

The study population included 75 females who had seeking in IVF at Al-Basma fertility Center in Gaza City, Gaza Strip. The mean age was 29.2±5.9 years. Clinical data showed that the majority of the interviewed woman 46 (61.3%) claimed that their husbands were the main cause of infertility. Around half of population 38 (50.7%) had undergone repeated IVF. The result of IVF was positive in 27 (36.0%) of the study population.

As indicated in table I, the age was classified into three categories: d”25, 26-35 and >35 years. The total number of oocytes was significantly decreased with increasing age registering means of 11.0±3.8, 9.3±5.7 and 5.8±5.6, at age groups d”25, 26-35 and >35 years, respectively (F=3.932 and P=0.024). This inverse relationship was exhibited in mature oocytes and number of embryo , but the change in their mean number among the different age groups was not significant. Pearson correlation test exhibited negative significant correlation between women age and the number of mature oocytes (r=-0.276, P=0.017) figure (1).

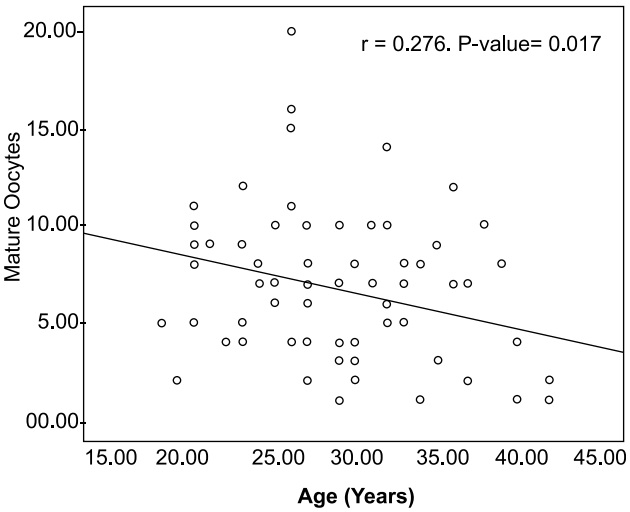

Fig.-1. *Correlation between women age and the number of mature oocyte.*

Table-I

Age classes of the study population in relation to various types of oocytes and embryos (n=75)

Oocytes	Age (year)			F	P-value
	(<25) (n=20)	(26- 35) (n=42)	(> 35)(n=13)		
Total number of oocytes	11.0±3.8	9.3±5.7	5.8±5.6	3.932	0.024
Mature oocytes	7.4±2.7	7.0±4.2	4.5±3.8	2.488	0.090
Immature oocytes	4.1±2.7	2.7±2.6	1.5±2.3	3.971	0.023
Number of embryo	3.9±1.3	3.6±1.6	2.9±1.6	1.781	0.176

All values are expressed as mean ±SD.

P- value less than 0.05 was considered for statistical significance

P- value more than 0.05 was not considered for statistical significance

Table II

Age of the study population in relation to ovarian response during IVF program (n=75)

Ovarian response	No.	(%)	Age (year) (mean ± SD)	F	P-value
Poor responders(<4 oocytes)	15	20	33.4±6.5	6.773	0.001
Normal responders(4-8 oocytes)	21	28	30.2±4.5		
Good responders(9-16 oocytes)	32	42.7	26.7±5.0		
High responders(>16 oocytes)	7	9.3	27.7±4.9		

All values are expressed as mean ±SD.

P- value less than 0.05 was considered for statistical significance.

F: ANOVA test.

According to the number of oocytes retrieved upon stimulation by menotrophin (FSH 75IU, LH 75 IU), the study population was divided into poor, normal, good and high responders (Table II). Fifteen (20%), 21 (28%), 32 (42.7%) and 7 (9.3%) women gave <4, 4-8, 9-16 and >16 oocytes during ovarian stimulation of IVF program, respectively. When related to women age, the total number of oocytes was generally increased with decreased age, showing <4, 4-8, 9-16 and >16 oocytes at mean ages of 33.4±6.5, 30.2±4.5, 26.7±5.0 and 27.7±4.9 years, respectively. This inverse relationship between the total number of oocytes and age was found to be significant (F=6.773 and P=0.001), implying that younger women yield more oocytes.

Table III shows the relationship between women age and IVF outcome. Positive pregnancy occurred in women aged 26.7±4.1 years whereas negative pregnancy and no cleavage occurred at ages 30.6±6.4 and 32.0±4.2 years, respectively. When related to women age, IVF outcome showed that the chance of getting pregnant increased with decreased age (F=4.278 and p= 0.018).

Table III

Age of the study population in relation to IVF outcome during IVF program (n=75)

IVF outcome	Age (year) (mean ± SD)	F	P-value
Positive**	26.7±4.1	4.278	0.018
Negative***	30.6±6.4		
No cleavage	32.0±4.2		

All values are expressed as mean ±SD.

P- value less than 0.05 was considered for statistical significance.

F: ANOVA test.

Positive: pregnancy occurred, Negative: no pregnancy.

Discussion

The results of this study indicated that the majority of women in the Gaza Strip seeking IVF when their husbands had fertility problems and the process of pregnancy is delayed. A total 75 women was enrolled in IVF programs. The mean age of women (29.2 years) was close to that reported in Egyptian (29.0 years), Iranian (29.1 years) and Palestinian (28.7 years) studies,[13,15,16] but lower than that reported from the USA and South Korea (34.0 years).[17,18] The younger women seeking IVF in developing countries, including Gaza Strip, could be explained in the context of social habits where most families have the desire to have children immediately after marriage and they encourage women to undergo IVF. This is supported by the finding that around half of the study population had undergone repeated IVF. The outcome of IVF was positive in 36.0% of the study population. This finding was in agreement with the results of studies from the Netherlands and South Korea which showed that 36.0% and 32.5% of women undergoing IVF achieved viable pregnancy.[17,19] However, the pregnancy rate among patients who had an IVF trial in different settings was 23.1%. Nevertheless, IVF treatment outcome is highly variable and difficult to predict.[15]

Data of the present study revealed an inverse relationship between women age and various types of oocytes, and embryo, with significant change detected with the total number of retrieved oocytes. Similar results were obtained.[3,13,17,20] Such decrease in the total number of oocytes with aging may be related to increase basal level of FSH which results in diminishing ovarian reserve and to the responsiveness of women in IVF program.[21,22] In this context, Pearson correlation test showed negative significant correlation between age and the number of mature oocyte. This result is in concurrent with that previously reported.[13,20]

Ovarian response was diminished with aging, showing poor response (<4 oocytes) at the mean age of 33.4±6.5

years and good response (9-16 oocytes) at the mean age of 26.7±5.02 years. This means that younger women have a better chance of a successful IVF. Studies carried out on ovarian reserve and ovarian response in *IVF* women found that the poor responses were detected at mean ages 36.3 and 32.5 years[23, 24]. This inverse relationship between ovarian response and female age was also documented in other studies.[13,16,20] The IVF outcome showed that the youngest women (mean age 26.7±4.1 years) had a better opportunity to get pregnant. This is supported by the aforementioned finding that ovarian response increased with decreasing age making more chance for pregnancy to occur. In addition, this finding coincides with other studies who found that pregnancy outcome of IVF program was significantly higher in younger women than that in the older ones.[13,25] Similar findings were also reported,[19] but the difference in the pregnancy outcome of IVF program was not significant**.**

Conclusion

In conclusion, the total number of retrieved oocytes, ovarian response and the chance of getting pregnancy were diminishing with ageing. Therefore, it is important to consider maternal age during IVF program.

Conflict of Interest: None

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