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## Determining fertility rate in women using Assisted Reproductive Techniques (ART) and aged > 38 years in Montaserieh infertility center, Mashhad

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### ABSTRACT

The struggle for the treatment of infertility has long been a major issue in medicine. But fertility rate naturally decreases in women with age and also in those using Assisted Reproductive Technology (ART). The purpose of this study was to determine fertility rate in women undergoing ART and aged > 38 years. In this cross-sectional study, 150 patients with infertility aged > 38 years, who had referred to Mashhad Montaserieh hospital for treatment by IVF from 2009 to 2014, were evaluated. The results were evaluated using a questionnaire including age of the patient and her husband, the cause and duration of infertility, spermogram, the number of treatment cycles, the number of used ampoules, the number of retrieved oocytes, the number of transferred embryos, the result of treatment, and the results of pregnancy. The analysis was carried out using SPSS statistical software, T-test, and Chi-square test. A value of  $P < 0.05$  was considered statistically significant. The mean age of women and their husbands was higher in the group with treatment failure than in patients with successful ART, but the association was not statistically significant. Shorter infertility duration and multifactorial infertility were associated with better treatment response, but that too was not statistically significant. There was no significant difference between the two groups in terms of the number of previous treatment cycles and the number of used ampoules. Increased number of retrieved oocytes was related with increasing successful fertility rate, but was not statistically significant. Increased number of transferred embryos was significantly associated with successful fertility rate. The success rate of ART was 7.3%. Infertile couples' age is one of the most important factors in the success of ART; therefore, it is recommended that with better information, the eligible patients be treated at an early age.

### Introduction

Having a child is the natural and inalienable right of every couple. Attention to the causes of infertility and trying to solve this problem was always important, but with the beginning of a new period of treatment using IVF in recent years, and the progress of science, biology, reproduction, and cellular-molecular changes, the use of new methods of treatment of infertility is common(1). Increased life expectancy, advanced age of marriage, various socio-economic factors, and an

overall change in the role of women in the society has led to couples having children at a later age. During recent years, the increased accessibility to ART has increased the chance of older parents with poor pregnancy outcomes to conceive children, hence, increasing the mean paternal age at first childbirth (2, 3). The mean maternal age has been increased by approximately 5 years between the periods of 1965–1969 and 1995–1999 (4). In comparison to 1993, the paternal age of English fathers has increased by 15% in a period of ten years (5). Moreover, it is increasingly

common for women in many countries to delay childbearing until the age of 35 years or older (6). Also, the women's tendency toward deferred childbirth has risen steadily since ART treatments for infertility became available in 1980 (7). Fertility decreases with increasing age after approximately 30 years of age, with an accelerated decline in fertility in women aged between 30 and 35 years (8). Therefore, delayed childbearing reduces the chance of a spontaneous pregnancy (9, 10).

In addition, delayed childbearing and increasing age have resulted in increasing the number and proportion of women aged  $\geq 35$  years who are seeking ART treatment (11). Unfortunately, the outcomes of ART treatment are also adversely affected by advanced maternal age, and it is becoming increasingly important to optimize ART treatment outcomes for these women (12). Therefore, this study was performed with the aim to determine fertility rate in women undergoing ART and aged  $> 38$  years.

## Materials and Methods

This cross-sectional study was performed on 150 patients with infertility, aged  $> 38$  years, who had referred to Mashhad Montaserieh hospital for treatment by IVF from 2009 to 2014. Sampling method was easy sampling. At first, according to the objectives of the study and based on the available variables, the questionnaires were designed to obtain information of each patient. Data collection tool was a questionnaire that was filled by the section's intern. The questionnaire included patient's name, age, husband's age, duration of infertility, cause of infertility, number of successful treatment cycles, the number of used ampoules, used medications, number of retrieved oocytes, the number of transferred embryos, husband's spermogram, treatment outcome based on HCG test, and pregnancy outcome based on the birth of alive child. Next, the information of all the people who had referred to Mashhad Montaserieh infertility center for IVF was collected. All personal information, medical information, and the results of treatment for each patient were separately entered to the questionnaire. After collecting and compiling data from all completed

questionnaires, data were analyzed using SPSS software, T-test, and Chi-square tests. P value  $< 0.05$  was considered statistically significant.

## Results

In this study, mean age of all the studied patients was  $39.91 \pm 2.207$  years (minimum 38 and maximum 49 years). The mean age of the patients with a positive treatment outcome based on BHCG test was  $38.73 \pm 1.272$  years and in patients with a negative result, it was  $40.01 \pm 2.241$  years. T-test showed that there was no significant difference between the two groups in terms of mean age ( $P = 0.064$ ).

The mean age of all patients' husbands was  $43.15 \pm 5.399$  years (minimum age 27 and maximum 65 years). The average age of husbands of patients with positive HCG treatment outcome was  $40.55 \pm 2.622$  years and in patients with negative treatment, outcome was  $43.36 \pm 5.513$  years. T-test showed that there was no significant difference between the two groups of patients in terms of husbands' age ( $P = 0.096$ ).

The mean duration of infertility in all the studied patients was  $9.39 \pm 6.713$  years (minimum 1 and maximum 26 years). The mean duration of infertility in patients with a positive treatment outcome was  $6.64 \pm 5.954$  years and in patients with a negative result, it was  $9.61 \pm 6.740$  years. T-test showed that mean duration of infertility was not significantly different between the two groups ( $P = 0.064$ ).

The most common cause of infertility in all the studied patients was male infertility as reported in 93.3% of all the patients. The most common cause of infertility in patients with a positive treatment outcome was multifactorial causes that involved 12.1% of all cases of multifactorial causes. The most common cause of infertility in patients with a negative treatment outcome was idiopathic causes that involved 100% of patients with idiopathic causes.

The mean number of treatment cycles in all the studied patients was  $1.03 \pm 0.162$  (maximum 2 cycles and minimum 1 cycle of treatment). The mean number of resulted treatment cycles in patients with positive treatment outcome was  $1 \pm 0$  and in patients with negative treatment

outcome, it was  $1.03 \pm 0.168$ . In total, 97.3% of the patients had 1 cycle and 2.7% had 2 cycles which had been resulted. T-test showed that the number of resulted treatment cycles was not significantly different between the two groups ( $P = 0.572$ ).

The mean number of ampoules used in each cycle for laboratory fertility in all the studied patients was  $45 \pm 16.156$  (minimum 8 and maximum 110 ampoules). The mean number of ampoules used in each cycle in patients with a positive result was  $42.27 \pm 10.011$ , and in patients with negative treatment outcome, it was  $45.22 \pm 16.551$ . T-test showed that there was no significant difference between the two groups of patients in terms of the mean number of ampoules used ( $P = 0.563$ ).

The mean number of retrieved oocytes in all the studied patients was  $4.65 \pm 3.697$  (minimum 1 and maximum 24). The mean number of retrieved oocytes in patients with positive treatment outcome was  $6.45 \pm 3.643$ , and in patients with a negative result, it was  $4.50 \pm 3.676$ . According to the T-test, the mean number of retrieved oocytes was not significantly different between the two groups ( $P = 0.092$ ).

The mean number of transferred embryos in all the studied patients was  $2.24 \pm 1.522$  (minimum 0 and maximum 5). The mean number of transferred embryos in patients with positive treatment outcome was  $3.18 \pm 1.328$ , and in patients with negative treatment outcome, it was  $2.17 \pm 1.516$ . According to the T-test, the mean number of transferred embryos was significantly higher in the group with positive treatment outcome than the group with negative treatment outcome ( $P = 0.033$ ).

Table 1: Evaluation of spermogram in the studied patients. Comparison of spermogram among the two groups according to the Chi-square test showed no significant difference between the two groups ( $P = 0.107$ ).

Table 1: Evaluation of spermogram in the studied patients

Spermogram	Treatment outcome N (%)	
	Negative	Positive
Favorable	54 (88.5)	7 (11.5)
Unfavorable	85 (95.5)	4 (4.5)
Total	139 (92.7)	11 (7.3)

In the evaluation of resulting pregnancy in all the studied patients, 11 of the patients (7.3%) had positive treatment outcome and 139 (92.7%) had negative treatment outcome.

In the evaluation of pregnancy outcome in all the studied patients, 3 cases (2%) had live births and 8 (5.33%) had pregnancies resulting in abortion. In total, 27.27% of patients with a positive treatment outcome had pregnancies resulting in live births.

## Discussion

It has been reported that the birth rate in women more than 40 years of age increased (aged 40–44 years) or remained steady (aged 45–49 years) compared with decreased birth rates in all age groups less than 40 years (13). In fact, the birth rate for women > 40 years of age has been the highest in more than four decades (13). The use of ART has increased the birth rates in women > 35 years, and even women > 45 years (14). Assisted reproductive technology has been associated with adverse pregnancy outcomes, including earlier delivery of pregnancies, low birth weight, very low birth weight, preterm delivery, and other potential complications associated with abnormal placentation (15, 16).

According to the result of this study, the outcome of fertility by ART based on BHCG test was positive in 7.3% ( $n = 11$ ) and negative in 92.7% ( $n = 139$ ) of the patients. Eleven cases had successful reproductive outcome of pregnancy. Pregnancy in 2% of the total patients led to live births and abortion was reported for 5.33% of the patients. The success rate of ART in other studies varied from 70–90%, which is much higher than that in our study. This is mainly due to the range of age of the patients in this study which was > 38 years, because according to the findings of other studies and the results of present study, age is one of the most important criteria to predict the outcome of ART. Of course, development of new methods of IVF in other countries should also be considered (17, 18).

The mean age in patients with positive treatment outcomes was 38.73 years and 40.01 years in the group with negative treatment outcomes; although maternal age was higher in the group which had failed treatment, but according to T-test, the difference was not

significant ( $P = 0.064$ ). Increased rate of treatment failure with increasing maternal age has been mentioned in various books and studies (19, 20).

Husband's age was also evaluated in this study. In patients with positive treatment outcomes, it was 40.55 years and 43.46 years in the group with negative treatment outcomes. Although as the case with maternal age, husband's age was higher in the group which had failed treatment, but, the difference was not significant ( $P = 0.096$ ). Increasing rates of treatment failure with increasing husband's age is reported in different studies (21).

In the current study, mean duration of infertility was 6.64 years in the group of successful treatment and 9.61 years in patients with treatment failure, although no significant difference was observed between the two groups ( $P = 0.158$ ). The impact of duration of infertility on the outcome of IVF is not clearly discussed, but the type of infertility has been studied and unexplained infertility with unknown cause has better response to treatment (22). In this study, the cause of infertility in both groups was evaluated and the highest success rate of treatment was observed in the multifactorial group (12.1%).

The present study showed that mean number of resulted treatment cycles and the number of ampoules used in each cycle were not significantly different in two groups. This issue is also evaluated in other studies and similar results were reported (23).

According to the results of this study, mean number of retrieved oocytes was 6.45 in patients with successful treatment and 4.5 in treatment failure group. The mean number of transferred embryos was 3.18 in successful pregnancy and 2.17 in the group with unsuccessful pregnancy. In other studies also, more retrieved oocyte and transferred embryo were associated with greater chance of success rate of pregnancy (22 and 23), but the likelihood of multiple pregnancy is also increased (24).

## Conclusions

Infertile couples' age is one of the most

important factors in the success of ART; therefore, it is recommended that with better information, the eligible patients should be treated at an early age.

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