

## Prognostic Factors of Pregnancy in 500 Cases of Intrauterine Insemination in Babol, Northern Iran

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### Abstract

**Background:** Intrauterine insemination (IUI) is a primary, simple and effective method of infertility treatment. The aim of this study was to determine the success rate of IUI and some related male and female factors.

**Materials and Methods:** This quasi - experimental study was done on 500 infertile couples from 2006 to 2008. Either clomiphene or human menopausal gonadotropin (HMG) alone or clomiphene with HMG was used for ovulation induction. Patients were subsequently followed by vaginal sonography. When at least one follicle of 16 mm or more in diameter was noted, patients were administered 5000 IU human chorionic gonadotropin (HCG) and 36 hours later, IUI was done. Age, duration of infertility, follicle number, treatment regimen, etiology of infertility and the outcome was recorded for every patient.

**Results:** In this study, the pregnancy rate was 19.6%. In pregnant women, the mean age was lower than non - pregnant women ( $p=0.004$ ). The mean duration of infertility in pregnant women was significantly lower than others ( $p=0.002$ ), but the number of dominant follicle, type of treatment regimen and etiology of infertility did not show significant differences between pregnant and non-pregnant women ( $p>0.05$ ).

**Conclusion:** The result of this study showed that etiology of infertility, type of treatment regimen for induction ovulation and the number of dominant follicles did not correlate with pregnancy occurrence in an IUI cycle, but the womens' ages and duration of infertility correlated with the occurrence of pregnancy.

**Keywords:** Intrauterine Insemination, Infertility, Pregnancy

### Introduction

Infertility is the failure of a couple to conceive after attempts for at least one full year (1). The high prevalence of infertility has become one of the major societal problems. Vahidi et al. has reported an infertility rate of 24.9% in Iran. In Mazandaran Province alone the rate of infertility is 22.4% (2). Intrauterine insemination (IUI) is the first effective treatment for suitably chosen patients. This method is less expensive and less invasive than other methods (3). IUI with or without ovulatory stimulation is used for specific infertility causes such as male factor disorders, inappropriate cervical mucus, presence of anti-sperm antibodies, mild endometriosis, ovulatory disorders which are resistant to primary treatment, and unexplained infertilities (4-6). The success rate of this method has been reported differently according to various studies and is dependent upon different factors. According to a study by Azargoon and Yousefi in Semnan Province, the pregnancy percentage per cycle in the IUI method was reported to be 13.6% (7).

In a Sadaghiani et al. study the rate of pregnancy for the patients who had ovulatory and male disorders was 11.1% and 7.1%, respectively (1). As mentioned in various studies, number of follicle, normal percentage of sperm morphology, maternal age (8-10) are effective conditions that determine the success of the IUI method.

It was reported that 300 infertile couples with an unknown cause of infertility underwent the IUI method in a Van Rumste study. There were no meaningful differences in pregnancy rate between the women with one, two, three or four follicles. The rate of pregnancy was high in the primary treatment cycles and decreased as treatment cycles increased (9). Maternal age was an effective factor for a successful IUI (10). Our infertility centers treat patients from nearby towns in Mazandaran Province, northern Iran. This study was designed in order to evaluate the results and determine effective factors in the IUI treatment cycles due to the lack of a thorough study of IUI results in our region.

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## Materials and Methods

This quasi - experimental study was undertaken on 500 infertile couples with different infertility causes who underwent IUI in Mehrgan and Fatemeh Zahra Infertility Centers at Babol University of Medical Sciences, Mazandaran Province, northern Iran from 2006 to 2008. The study was approved by the Ethics Committee at Babol University of Medical Sciences and written informed consent was obtained from all study subjects. Tubal and severe male disorders such as oligospermia, genitourinary anatomic disorders, ejaculation disorders and endocrine disorders were the exclusion criteria. A precise history was taken from all couples and all female participants underwent a thorough physical examination, clinical laboratory tests and hysterosalpingography. Seminal fluid analysis was done for all male participants using the Nordic Association for Andrology and European Society of Human Reproduction and Embryology guide. (NAFA - ESHRE) (11). The infertile cases with ovulatory disorders as well as , male and unexplained disorders participated in the study. On the basis of the NAFA - ESHRE guide, normal seminal fluid samples prior to washing are as follows:

1. Over 20 million per ml sperm count
2. Over 50% sperm motility
3. Over 25% progressive sperm (grade III and IV)
4. Over 50% vitality.

Specifications of normal semen fluid samples after washing are as follows:

1. Over 20 million per ml sperm count
2. Over 15% normal morphology
3. Over 75% grade III and IV sperm.

The main endpoint of our study was the occurrence of pregnancy.

Methods of ovulatory stimulation used in our study were:

1. Administration of 100 mg clomiphene citrate (CC) (Iran Hormone Company, Terhran, Iran) daily from the third day of patients' cycles up to five days.
2. Administration of CC and human menopausal gonadotropin (HMG+CC) (HMG, Merional, IBSA company, Switzerland). CC was administered from the third day until the seventh and intramuscular

injection of 75mg HMG from day six of patients' menstrual cycles up to three days which continued if necessary.

3. Muscular injection of 75mg HMG daily from the third day of patients' cycles up to five days, resuming the treatment if necessary depending on the follicular growth.

All patients were followed by vaginal sonography and when they had at least one dominant follicle (16-22 millimeters), 5000 units of human chorionic gonadotropin (HCG) was injected intramuscularly and after 36 hours, intrauterine insemination was done by injection of 0.3 to 0.5mL seminal fluid prepared in a swim up method by means of a val-lace catheter. The patients were then advised to perform a beta-hCG test 16 days after IUI if they had amenorrhea. The data included from the different causes of infertility were age, infertility duration, follicular count and type of treatment which were recorded in our questionnaires. The obtained data were analyzed by SPSS statistical software (version 12). Kolmogorov Smirnov test was used to determine sample normality. The normality of continuous variables (duration of infertility, number of follicles) was tested by the Kolmogorov Simirnov test. For comparison of mean values, the student's t-test or Mann - Whitney test were used. The chi square test was used for categorical variables. P values < 0.05 were considered significant.

## Results

This study was done on 500 intrauterine insemination cases, wherein 98 of the cases (19.6%) resulted in pregnancy. The male average age was  $26.8 \pm 6.2$  years and  $31.7 \pm 7.4$  for the females. The average age of the women with a positive IUI result was  $25.5 \pm 4.9$  years which was significantly lower ( $p=0.004$ ) The average duration of infertility was  $3 \pm 3.7$  years for all study participants. The follicle count and the duration of infertility are shown in table 1, based upon the IUI result. Ovulatory stimulation in 251 patients (50.2%) was done by CC, 14 (2.8%) by HMG and 235 (47%) by the CC+HMG as shown in table 2 on the basis of pregnancy occurrence.

*Table 1: Duration of infertility and number of follicles according to pregnancy in IUI cycles*

Variable	Pregnancy	Number	Median	(Mean $\pm$ SD)	P-value
Duration of infertility	+	98	2	$2.7 \pm 1.9$ (yr)	0.002
	-	402	3	$3.9 \pm 1.9$ (yr)	
Number of follicles	+	98	2	$2.2 \pm 1.4$ (yr)	0.178
	-	402	3	$2.1 \pm 1.3$ (yr)	

**Table 2: Frequency and percentage of pregnancy in different treatment regimens in IUI cycles.**

Treatment Protocol	CC *	HMG **	CC + HMG ***
<b>Pregnancy</b>	<b>Frequency (%)</b>	<b>Frequency (%)</b>	<b>Frequency (%)</b>
Positive	43 (17.1)	1 (7.1)	54 (23)
Negative	208 (82.9)	13 (92.9)	181 (77)
<b>Total</b>	<b>251 (100)</b>	<b>14 (100)</b>	<b>235 (100)</b>

$p=0.132$

\*CC \*: Clomiphene citrate

\*\* HMG: Human menopausal gonadotropin

\*\*\* CC + HMG: Clomiphene + human menopausal gonadotropin

There were no significant differences between the treatment groups in pregnancy percentage ( $p=0.132$ ) (Table 2). Ovulatory disorders were present in 276 patients (55.2%) while 186 patients (37.2%) had mild male disorders.

The pregnancy rate was 23.7% for unexplained infertility, 20.1% in ovulatory disorders, 20.2% in male disorders and 12.4% in male and female disorders, as seen in Table 3. There was no significant relationship between pregnancy occurrence and type of infertility ( $p=0.194$ ).

## Discussion

In this study pregnancy occurred in 98 (19.8%) of the infertility cases. In a Mehrafza et al. study undertaken on 336 IUI cycles, the overall pregnancy rate was 18.2% (12). In another study by Delgadillo et al. the pregnancy rate was 21.7% (13) which was similar to the results of our study. However, the success rate in some studies was a little lower than ours, about 12% (14 - 16). In a Houmard et al. study, the clinical pregnancy rate was 7.1% and the women's average age was 36 years. In that study, ovulatory disorder was present in only 8.7% of the patients (17). Therefore, older women whose husbands had male factor infertility were the main cause of infertility and lower pregnancy rates. These differences between our study and the others are probably due to the effects of different factors causing infertility, type of treatment. The women in our country who refer for infertility treatment techniques are younger which could be another cause for these differences.

In this study, the average age of the patients with positive IUI results was significantly lower ( $p=0.004$ ). In a Sahakyan et al. study, the pregnancy rate after IUI resulted in decreased fertility because of the increase in female age (18). In the Van Voorish et al. study in 2001 which was done to determine the pregnancy anticipative factors in *in vitro* fertilization (IVF) and IUI, the maternal age was determined as an independent factor in anticipating pregnancy result after IUI (19). In a Ghosh

et al. study, the pregnancy probability in patients over 30 years old was 0.51 times lower than patients who were 30 years old and below (20). A study by Tur et al. reported that pregnancies by IUI and IVF were related to maternal age (21). In a Montanaro Gauci et al. study it was determined that maternal age has a negative relationship with women's age (22). A comparison of our study with the other studies shows the effects of maternal age on the success rate of IUI, which was probably due to the negative effects of increased maternal age on both the zygote and fetus (23).

The results of our study showed that the positive IUI patients had lower duration of infertility than the other group ( $p=0.002$ ). In other words, the IUI success probability increased in women with lower infertility duration. In the study by Houmard et al., pregnancy percentage in women with less than three years infertility (9%) was significantly higher than the patients who were infertile for greater than three years (2.2%) (17). Also in Iberico's study, the lower infertility duration caused an increased pregnancy rate in the multiple logistic regression model (24).

Our study revealed that there were no significant differences in follicle count between the patients with positive and negative IUI results ( $p=0.178$ ). In Van Rumste's et al. study, there were no significant differences in pregnancy rate between women with one, two, three or four follicles (25), which was similar to our study. In a Houmard et al. study there was a significant relationship between the rate of pregnancy and follicle count, therefore the pregnancy percentage in patients with more than three follicles (9.1%) was higher than in patients with less than three follicles (4.6%) (17). The follicle count in the pregnant group was significantly higher than those who did not become pregnant in the other studies (21, 22).

The positive relationship between follicle count and IUI success could be due to the increased probability of follicular fertilization with injected sperm.

In this study, the differences in pregnancy percentage between treatment groups was not statistically significant ( $p=0.132$ ). In a Stewart study there were no significant differences in pregnancy rate between the CC and HMG groups (26). A study by Wang et al. determined the rate of pregnancy in patients who had received CC was 6.5%, 22.3% in the HMG group and 14.2% in patients who had received CC accompanied by HMG, which was not statistically significant (27). According to Sikandar et al. there were no differences in pregnancy rate between the three treatment regimens for ovulation induction (28). A comparison between the results of our study and the others revealed that the type of treatment regimen which was used for ovulation induction probably had no effect on IUI success because the treatment purpose was ovulatory stimulation. Therefore there were no differences in the probable result of IUI between each method that caused ovulation.

In our study the highest pregnancy rate was seen in the unexplained cause infertility group (23.7%) and the lowest pregnancy rates were seen in the cases who had both male and female disorders (12.4%). However there was no significant relationship between pregnancy occurrence and infertility causes ( $p=0.194$ ). The causes of infertility also did not impact the IUI success rate in other studies. (4, 13). In a study by Tay et al., the pregnancy rate in male cause infertilities was lower than infertilities due to ovarian disorders (29). Whereas, the pregnancy rate in women with ovarian disorder infertilities and male factor disorder were approximately the same in our study.

## Conclusion

In this study, pregnancy occurred in one fifth (20%) of the infertile cases. The pregnancy rate was related to maternal age and infertility duration. There was no relationship between the pregnancy rate and follicle count, type of treatment or infertility causes.

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