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Predictive Factors Affecting Outcome of Intrauterine Insemination: A Prospective Study

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Abstract	**Original Research Article**

Background: Intrauterine insemination (IUI) is the therapeutic process of placing washed spermatozoa transcervically into the uterine cavity for the treatment of cervical factor subfertility, male subfertility and unexplained infertility. This prospective study was done to identify the most important parameters with regard to IUI success that would provide important data for predicting the success of therapy and further help in planning subfertility treatment for couples. *Methods:* It was a prospective randomized, comparative study of 406 eligible couple fulfilling inclusion criteria and exclusion undergoing 512 controlled IUI cycles, in department of Obstetrics and Gynecology, SMS Medical College, Jaipur. Patients were randomly divided at cycle level, out of total 512 cycles, 260 cycles were allocated to Clomiphene citrate (CC) group and 252 cycles were allocated to Human Menopausal Gonadotropin (HMG) group. Insemination was then performed with washed semen after 36-40 hrs of injection human chorionic gonadotropin for triggering ovulation. The patient was then called after 2 weeks for pregnancy tests which, if positive was considered as clinical pregnancy. *Result:* Out of 512 cycles, 59 cycles were positive. The pregnancy rate was 11.52%. Endometrial thickness, preovulatory follicle number, significantly affected the pregnancy outcome. Factors like patient's age, Husband's age, BMI<25, bilateral patent tubes and decreased duration of infertility also positively affected the outcome. *Conclusion:* IUI is a successful treatment for appropriately selected cases of infertility. A knowledge of predictive factors may be of help to offer and counsel patients regarding success of treatment outcome in IUI.
Keywords: Intrauterine insemination, Human Menopausal Gonadotropin, Pregnancy rate, Infertility.

INTRODUCTION

Infertility is defined as the inability to conceive after 1 year of unprotected intercourse of reasonable frequency during childbearing age. In couples with cervical factor subfertility, male subfertility and unexplained subfertility intra-uterine insemination (IUI) is often the first step in the treatment cascade. IUI is easy to perform, cost effective and non-invasive technique. For these reasons, it is probably the most frequently performed treatment in daily fertility practice. It is an intermediate procedure between the simpler ovulation induction and the more advanced in vitro fertilization especially in developing countries where the cost of treatment of IVF is a major issue. Several factors such as maternal age, paternal age, BMI, etiology of infertility, follicle number, endometrial thickness, semen parameters, patency of the tubes, timing of IUI and the number of IUI cycles have been studied to find out their effect on IUI results.

The objective of our study was to assess various predictive factors affecting pregnancy outcome in IUI.

MATERIALS AND METHODS

It was a hospital-based randomized comparative study was conducted prospectively in the Department of Obstetrics and Gynecology, SMS Medical College, Jaipur from April 2017 to October 2018 in which a total of 406 eligible couple fulfilling inclusion criteria were enrolled in the study. Inclusion criteria included patients suffering from unexplained and mild male factor infertility, minimal and mild endometriosis, ovulatory dysfunctions, ejaculatory failures and atleast one patent fallopian tube. Exclusion criteria included patients with severe oligozoospermia, bilateral tubal obstruction and intrauterine abnormality. After taking a written informed consent, history, detailed clinical examination and relevant investigations, patients were randomly divided at cycle level into two groups using COIN TEST.

260 cycles were allocated to CC group and 252 cycles were allocated to HMG group. Patients allocated to CC group received clomiphene citrate 50mg orally once daily from third day of cycle for five consecutive days. In CC group, estradiol valerate was added from day 8 until day 12 in the dose of 2mg -4mg /day to support endometrial growth. Injection HCG 5000-10000 IU was given to trigger ovulation when the diameter of the leading follicle was approximately 18-20mm.

A two layer gradient technique was used for sperm preparation. Insemination with washed husband's sperm was performed about 36-40 hours after HCG administration with 0.5 ml of inseminate. Patients were called after 2 weeks for pregnancy test. All patients underwent single insemination per cycle. The clinical pregnancy rate was calculated using Z test. Software used was SPSS 18.0. P value <0.05 was taken as significant.

RESULTS
406 patients attending the infertility clinic, after applying both inclusion and exclusion criteria were enrolled in the present study. Out of total 512 cycles, 59 cycles had a positive outcome.

The mean value of various variables affecting the treatment outcome according to the distribution of cases has been depicted in Table-1. Majority (45.52%) of the pregnancies occurred in the age group of 26-30 years. The mean age of patients in positive outcome group was 27.50±2.84 years in CC group and 27.22±3.44 years in HMG group as compared to 29.88±3.60 years and 30.06±3.52 years in the negative

outcome cycles in CC group and HMG group respectively. Younger age of the patient was associated with better pregnancy outcome.

BMI <25 was also associated with better pregnancy outcome. The pregnancy rate was higher in the BMI <25,which was 10.59% and 18.29% in CC and HMG group respectively and as compared to the BMI ≥25, which was 4.44% and 7.95 % in CC and HMG group respectively.though the difference was not statistically significant (p=0.144) in CC group and significant in HMG group (p=0.043).

The pregnancy rate was higher and statistically significant in patients who had development of 2 follicles (CC=54.54%; HMG= 54.05%) compared to those with monofollicular development (CC= 36.36%; HMG=43.24%%), p=0.006. The pregnancy rate was higher in patients with bilateral tubes patent (93.35%) compared to those with only one tube patent (6.64%), though the difference was not significant statistically, p=0864. The mean duration of infertility in the positive v/s negative outcome cases was 5.14±1.59years v/s 7.13±2.18years (p=0.001) in CC group and 5.21±1.52 years v/s 6.87±2.27 years in HMG group (p<0.001). Thus lesser duration of infertility was associated with better pregnancy outcome. The mean ET of positive outcome cases compared to negative outcome cases in CC group was 7.95±0.91mm v/s 7.6±0.73mm (p=0.039) and in HMG group it was 8.69±0.58 in positive cycles v/s 8.61±0.63 in negative cycles. Thus increased endometrial thickness was positively associated with better pregnancy outcome, which was also significant statistically.

Table-1: Mean values of various variables according to their distribution in the study

Parameters	Mean	
	CC	HMG
Patient's age (in years)	29.86±3.57	29.76±3.65
Husband's age (in years)	32.05±3.03	31.90±3.44
Patient's BMI	23.91±2.9	24.08±2.53
Duration of infertility (in years)	6.67±2.22	6.51±2.26
Preovulatory follicle no. (on the day of hCG injection)	1.67±0.87	1.43±0.78
Endometrial thickness in mm (on the day of hCG injection)	7.64±0.73	8.65±0.61

Table-2: Mean values of various variables according to the outcome in CC group

Variables	CC				
	Positive (15)		Negative (103)		p-value
	Mean	SD	Mean	SD	
Patient's Age (in yrs)	27.50	2.84	29.88	3.60	0.003
Duration of Infertility (in yrs)	5.14	1.59	7.13	2.18	0.001
Endometrial Thickness (in mm)	7.95	0.91	7.6	0.73	0.039

Table-3: Mean values of various variables according to the outcome in HMG group

Variables	HMG				
	Positive (15)		Negative (103)		p-value
	Mean	SD	Mean	SD	
Patient's Age (in yrs)	27.22	3.44	30.06	3.52	0.001
Duration of Infertility (in yrs)	5.21	1.52	6.87	2.27	0.001
Endometrial Thickness (in mm)	8.69	0.58	8.61	0.62	0.474

Table-4: Pregnancy Rate According to BMI

BMI	CC			HMG		
	Total	Positive	Pregnancy Rate (%)	Total	Positive	Pregnancy Rate (%)
<25	170	18	10.59%	164	30	18.29%
>=25	90	4	4.44%	88	7	7.95%
P-value	0.144			0.043		

Table- 5: Preovulatory follicle number and the pregnancy outcome

Preovulatory Follicle No.	CC			HMG		
	Total	Positive	Pregnancy Rate (%)	Total	Positive	Pregnancy Rate (%)
1	134	8	5.97%	180	20	11.11%
2	94	12	12.77%	56	16	28.57%
3	17	2	11.76%	7	1	14.29%
P-value	0.193			0.006		

Test: Chi-square test for goodness of fit

DISCUSSION

With the current trend of increasing infertility in population there has been more research over assisted reproductive techniques aimed to cater to need and resources of the general population. There are few unambiguous determinants of success that the clinician should be aware of to be able to provide couples with appropriate counseling. Our study has tried to predict various factors affecting the positive outcome of IUI. IUI is frequently offered to couples with problems conceiving, provided the woman has atleast on patent fallopian tube and her partner has only mildly altered semen quality.

Young age was associated with better pregnancy outcome as found by Dinelli L *et al.* [1] in their study. Aging is associated with progressive follicular depletion and diminished oocyte quality, which is accompanied by a reduction in the size or activity of the cohort of follicles available to respond to clomiphene citrate stimulation. This negative impact on treatment outcome may be due to the higher rate of aneuploidy found in dysmorphic oocytes. Nuojua-huttunen *et al.* [2] reported a pregnancy rate of 13.7% per cycle for a total 0f 811 IUI cycles in women up to the age of 40, and a rate of 4.1% thereafter. Souter *et al.* [3] described the impact of BMI on IUI cycles .In our analysis; BMI significantly affected the pregnancy rate. Our results would indicate that in women with overweight that undergo treatment for anovulation, the likelihood of achieving pregnancy decreases significantly. Lifestyle changes, exercise and weight loss are key factors in successfully treating infertility in such patients.

Increase in pregnancy rate with an increase in the number of preovulatory follicles is explained by the fact that multifollicular development may result in an increased number of fertilizable oocytes and a better quality endometrium and luteal phase, thus improving fertilization and implantation rates. This finding is supported by studies done by Dinelli L *et al.* [1], Yavuz A *et al.* [4] and Ashrafi M *et al.* [5]. Decreased duration of infertility was also associated with improved pregnancy outcome as found by Ashrafi M *et al.;* [5] in their study. We observed that pregnancy rate fell as the duration of infertility of increased, suggesting that other more complex assisted reproduction techniques should be used after five years of infertility.

Increased endometrial thickness was associated with a significant increase in the pregnancy outcome in IUI. Similar results were found in studies done by Dinelli L *et al.* [1], Wolff EF *et al.* [6] and Habibzadeh V *et al.* [7].

Thus IUI was found to be a better assisted reproductive option with significantly improved pregnancy rate and cost benefits. Endometrial thickness, preovulatory follicle number, significantly affected the pregnancy outcome. Various other variables like patient's age, BMI, tubal patency and duration of infertility also positively affected the treatment outcome.

CONCLUSION

In this study aimed at identifying factors that predict pregnancy following IUI, we found that the probability was greatest for couples composed as follows: women aged less than 35 years, with a BMI of 25 or less, with an infertility duration of less than 6 years and higher in cycles showing development of at least 2 follicles. Endometrial thickness also significantly affects the positive outcome. Thus, these predictive factors must be taken into consideration before offering and counseling patients about treatment outcome in patients undergoing IUI as a method of assisted reproductive technique.

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