



PREDICTIVE FACTORS FOR PREGNANCY AFTER INTRAUTERINE INSEMINATION: A PROSPECTIVE STUDY OF FACTORS AFFECTING OUTCOME

Gynaecology

SHARMA ANITA	Assistant Professor (Obstetrics and Gynecology) Zenana Hospital attached to SMS Medical College
MENGHANI REKHA	Junior Specialist (Obstetrics and Gynecology) Zenana Hospital attached to SMS Medical College
MAMTA MEENA	Assistant Professor, Department of Obstetrics and Gynecology, SMS Medical College, Jaipur
Dr. MENGHANI REKHA	Corresponding Author : 2/52, Malviya Nagar, Jaipur-302017

ABSTRACT

Objective: To determine the predictive factors for pregnancy after controlled ovarian hyperstimulation (COH)/intrauterine insemination (IUI).
Design: Prospective observational study.

Patients and methods: In 220 couples 365 stimulated IUI cycles between November 2013 and December 2014 at SMS Medical college, Jaipur (Obs & Gynae deptt).

Interventions: Ovarian stimulation with clomiphene citrate/CC+ gonadotrophins was initiated and a single IUI was performed 36 h after triggering ovulation.

Main Outcome Measures: The primary outcome measures were clinical pregnancy and live birth rates. Predictive factors evaluated were female age, duration of infertility, indication for IUI, number of preovulatory follicles, Endometrial Thickness on the day of Trigger, postwash total motile fraction (TMF).

Results: The mean age of females was 28.6 & mean ET was 8.1mm $\pm$ 1.47. The overall clinical pregnancy rate was 14.5%. The highest pregnancy rates (25%) obtained in cases anovulation due to PCOS with Gonadotrophins stimulation.

With increasing number of 16-18 mm follicles, difference in pregnancy rate was 16%, & 12% with 1-2 & >2 follicles respectively and was not significant. Pregnancies rates per cycle was significantly higher with the Donor sperm (22.4%) than when partner sperm was used (12.7%). (p<.05)

Conclusion: Among the predictive factors evaluated, following IUI donor sperm, ovulation induction protocols (use of gonadotrophins) Endometrial thickness (ET) >6mm influenced the clinical pregnancy rate.

KEYWORDS:

Intrauterine insemination, Pregnancy rate, Predictive factor, Gonadotropin

Introduction

Intrauterine insemination (IUI) is the first therapeutic step in assisted reproductive techniques and many factors, including male and female infertility and technique-dependent factors, have been reported to influence pregnancy rates after IUI. Intrauterine insemination (IUI) indicated for unexplained subfertility, minimal-mild endometriosis, male subfertility and physical disability or psychosexual problems, is widely used as first line treatment for subfertile couples.

Material & Methods

Overall, we analyzed 365 IUI cycles at SMS Medical College Jaipur (Dec 2013 to Nov 2014). A basic infertility study was performed before starting controlled ovarian hyperstimulation (COH). The study consisted of medical history, physical examination, transvaginal ultrasonography, hormone study, Diagnostic laparoscopy/ hysterosalpingogram and semen analysis. The hormones studied were follicle stimulating hormone (FSH), luteinizing hormone (LH), prolactin (PRL). Cycles were natural/stimulated with clomiphene citrate and/or gonadotrophins (HMG/FSH), 50-100 mg clomiphene citrate (D3-D7), followed by 75-150 IU of gonadotrophins added. Ovarian (Follicle maturation) and endometrial responses monitored by serial TVS on the ninth day of stimulation and repeated after 2 or 3 days, depending on the follicular growth. 5000-10000 IU HCG administered (when at least one follicle mean diameter was >18 mm). On the day of hCG administration, TVS scan measure endometrial thickness (ET) & Measurements made from the outer edge of the endometrial-myometrial interface to the outer edge in the widest part of the endometrium. In this study, we evaluated endometrial thickness within 3 ranges of ≤ 6 , $6 < ET \leq 10$ and > 10 mm. Standard IUI one 36 hours after administration of hCG. The administration of hCG was withheld, IUI canceled when >3 follicles with a diameter of at least 16 mm / >4 follicles with diameter of at least 14 mm present. The specimen collected after liquefaction and initial sperm analysis. Semen preparation for IUI was performed with the density gradient centrifugation technique (10 minutes at 1500 rpm) and a washing step (10 minutes at 1500 rpm) with 2-ml culture medium. Luteal phase was

supported by daily vaginal administration of 200 mg natural micronized progesterone for 14 days. Plasma β -hCG levels done 2 weeks after IUI. Clinical pregnancy was defined as TVS visualization of intrauterine gestational sac(s).

Results

In 220 couples, 365 cycles performed, out of which 52 had UPT positive after 15 days. In this study Pregnancy rate was 14.5% (52/365), 90% (47/365) of pregnancies were ongoing and 5/365 cases had missed abortion. On the basis of etiology, Couples treated for anovulation associated with PCOS & Azoospermia had the highest pregnancy rate per cycle were 26%. The lowest pregnancy rates were obtained for endometriosis (5.8%) (table no.1)

About 294 cycles were of primary infertility while 71 cycles were of secondary infertility. (Table no.2) There was no significant difference in the pregnancy rate in cases of primary (13.6%) and secondary infertility (16.9%) group (p value > 0.503 NS). Our study shows no significant difference in pregnancy rates according to whether the length of infertility was below or above 6 years (16.8% vs 10.8%). (Table 2) There was a decreasing trend in pregnancy rates/cycle with increasing age from 16% in <25 years age to 14% in age group of 26-35 years and 8.7% in the age group of >35 years (Table 3) though the difference was not significant (P Value > .05)

With increasing the number of 16-18 mm follicles pregnancy rate was 16%, 12% with 1-2 follicles and >2 follicles respectively & was not significant (Table 4) Of all participants in the study, 145 (39.2%) had clomiphene citrate & 131 (35.8%) in the letrozole group and 67 (18.3%) were on Letrozole + gonadotrophins or Clomiphene + gonadotrophins had pregnancy rates of 13.7%, 18.9% and 25% respectively. clinical pregnancy rates were much higher in gonadotrophins group. This difference in gonadotrophins group was significant (p value < .05) (Table 4)

The mean ET in age range 17-25 yrs was 7.4 $\pm$ 1.98 mm and in age range

of >40 years was 6.9±1.7 mm (Table) Approx. 90% of cases with pregnancy test positive had endometrial thickness in the range 6-12mm on the day of trigger. (Table 5) In all age ranges, pregnancy rate was lower with ET≤6 mm

According to male factor ,IUI with the husband semen done in 298 cases, (81%)&donor semen in azoospermia in 67cases(19%).If we only consider the number of spermatozoa & their motility, our study does not show any significant difference according to these parameters, as long as they are normal. The fact that donor sperm is of higher quality explains the pregnancies rates per cycle was significantly higher (22.4%) than when partner sperm was used (12.7%). (Table 6). (P value<.05).In our study, the mean number of IUIs per couple was 1.6, observed that the highest pregnancy rate(58.4%) occurred in the first cycle . (Table 6)

Discussion

According to the practice committee of ASRM guidelines ,basic infertility workup included ovulation assessment, hysteros alpingogram, husband semen analysis, uterine cavity assessment, and, if indicated, tests for ovarian reserve and laparoscopy (1)

In our study, in cases with female etiology, pregnancy rate was much lower in endometriosis case(5.85%) Similarly Toma and Hammond (2) reported a pregnancy rate of 6.5% per IUI cycle for donor sperm in women with stage I-II endometriosis compared to 14% in the control group. (Table 1) Hansen et al, Kamath et al., Tomlinson et al., and Ashrafi et al. in their independent studies found prolonged duration of infertility to be associated with decreased success rate. Similar to the present study,Zainul et al. and Tay et al. did not find any significance associated with duration of infertility(4, 9-11].(table 2)

Age of the couple, especially female age, (Table 3) has been found to be an important predictor in many studies like Montanaro Gauci et al. in 2001 and AMIGOS trial in 2016 (3,4). However, many studies have documented a significant drop in the success rate beyond the age of 40 years, with reported live births being as low as 1.4% (5,6,7) Macizo et al (8) studied the pregnancy rates / cycle for age brackets <30 years, 30 - 35 years, and 35 - 40 years, were 11.4%, 10.6%, and 9.6%, respectively & the woman's age did not significantly affect the pregnancy rate.In present study, there were no significant differences between the three age groups regarding clinical pregnancy or endometrial thickness .(Table 5)

In our study the number of dominant follicles did not influence the pregnancy rates Macizo et al(8), the number of pre-ovulatory follicles recruited was observed to be a significant factor . Similar to our study, (table 4)Karen Peeraer et al(12) compared ovarian stimulation with hMG versus CC, hMG stimulation was characterized by a higher clinical pregnancy rate (hMG 14.4%) v/sCC 9.0%).

In our study, the mean number of IUIs per couple was 1.6. There is evidence suggesting that the number of IUI trials should be limited to 3 as the pregnancy rate per cycle is very low after the 3rd cycle (Table 6)

Conclusion

This study reviewed the impact of various prognostic factors on the pregnancy rate in cases of infertility, so that it can help in counselling patients as well as deciding the appropriate treatment option available based on patient factors.

Table 1 Distribution of cases according to the etiology

Etiology	No. of cycles %(n)	Clinical Pregnancy %(n)	Ongoing %(n)	Missed %(n)
Male	19.7(72)	20.8(15)	20.8(15)	0
PCOS	22.7(83)	24.7(20)	20.4(17)	3
Endometriosis	4.6(17)	5.8(1)	0	1
Unexplained	47.6(17)	9.7(17)	9.1(16)	1
M+PCOS	5.2(9)	26.3(5)	26.3(5)	0

Table 2

	No. of cycles %(n)	Clinical Pregnancy %(n)	Ongoing %(n)	Missed %(n)	p value
Duration of infertility					

<=6 yrs	57%(208)	16.8%(35)	14.9%(31)	4	0.284 NS
>6 yrs	43%(157)	10.8%(17)	10.1%(16)	1	
Type of infertility					
Primary	294(80%)	13.6%(40)	12.5%(37)	3	0.503
secondary	71(20%)	16.9%(12)	14%(10)	2	

Table 3

Female Age(yrs)	No. of cycles %(n)	Clinical Pregnancy %(n)	Ongoing %(n)	P value
17-25	86	1614(1)	13(11)	0.521
26-35	255	14(36)	13(34)	
36-40	23	8.7(2)	0	
>40	1	0	0	

Table 4

Dominant follicles >16-18 mm	cycles (n)	Pregnancies (n)	Rate/cycle %	P value
1-2	212	34	16	.521 NS
>2	153	19	12	
Stimulation				
Letrozole	131	18	13.7	<.05
Clomiphene citrate 50/100	145	12	12	
Letrozole/CC+gonadotrophins	67	17	25	
Natural	22	5	23	

Table no.5 Relationship of ET and Pregnancy rates

ET mm	No. of cycles n	No. of pregnancies/ cycles n(%)	ongoing	missed	P value
<6mm	17	1/17(5.8)	2	0	0.284
6-<8mm	140	18/140(12.8)	16	1	
8-<10 mm	1173	24/173(13.8)	21	3	
10-<12 mm	23	5/23(21.7)	4	1	
>=12 mm	12	4/12(33.3)	4	0	
Total	365	52/365(14.5)	47	5	

Table 6

Technique dependent factors	cycles (n)	Pregnancies (n)	Rate/cycle %	P Value
Type of insemination				
IUI-partner	298	38	12.7	0.033
IUI-donor	67	15	22.4	
No. of IUI cycles				
1	212	3	58.4	
2	102	13	24.5	
3	38	8	15	
4	13	0	0	

References

1. The Practice Committee of the American Society for Reproductive Medicine, "Effectiveness and treatment of unexplained infertility," Fertility Sterility, vol. 86, no. 5, pp. S111–S114, 2006.
2. Toma SK, Stovall DW, Hammond MG. The effect of laparoscopic ablation or danocrine on pregnancy rates in patients with stage I or II endometriosis undergoing donor insemination. Obstet Gynecol.1992;80(2):253-6.
3. M. Montanaro Gauci, T. F. Kruger, K. Coetzee, K. Smith, J. P. Van Der Merwe, and C. J. Lombard, "Stepwise regression analysis to study male and female factors impacting on pregnancy rate in an intrauterine insemination programme," Andrologia, vol. 33, no. 3, pp. 135–141, 2001
4. K. R. Hansen, A. L. He, A. K. Styer et al., "Predictors of pregnancy and live-birth in couples with unexplained infertility after ovarian stimulation-intrauterine insemination," Fertility and Sterility, vol. 105, no. 6, pp. 1575–1583, 2016.
5. M. Aboulghar, R. Mansoure et al, "Controlled ovarian hyperstimulation and intrauterine insemination for treatment of unexplained infertility should be limited to a maximum of three trials," Fertility and Sterility, vol. 75, no. 1, pp. 88–91, 2001.
6. Y. Tay, V. R. Raj, A. Kulenthiran, and O. Sitizawiah, "Prognostic factors influencing pregnancy rate after stimulated intrauterine insemination," Medical Journal of Malaysia, vol. 62, no. 4, pp. 286–289, 2007.
7. G. Ibérico, J. Vioque, N. Ariza et al., "Analysis of factors influencing pregnancy rates in homologous intrauterine insemination," Fertility and Sterility, vol. 81, no. 5, pp. 1308–1313, 2004.
8. Macizo Soria et al Pregnancy Predictors following IUI I J Reprod Infertil. 2012;13 (3):158-166)
9. M. S. Kamath et al., "Predictive factors for pregnancy after intrauterine insemination: a prospective study of factors affecting outcome," Journal of Human Reproductive Sciences, vol. 3, no. 3, pp. 129–134, 2010.

10. M. J. Tomlinson, J. B. Amissah-Arthur, K. A. Thompson, J. L. Kasraie, and B. Bentick, "Infertility: prognostic indicators for intrauterine insemination (IUI): statistical model for IUI success," *Human Reproduction*, vol. 11, no. 9, pp. 1892–1896, 1996.
11. M. R. R. Zainul, F. B. Ong, M. H. Omar et al., "Predictors of intrauterine insemination success," *Medical Journal of Malaysia*, vol. 61, no. 5, pp. 599–607, 2006.
12. Karen Peeraer, Sophie Debrock, Peter De Loecker, et al., Low-dose human menopausal gonadotrophin versus clomiphene citrate in subfertile couples treated with IUI: a RCT *Hum Reprod* (2015) 30 (5): 1079-1088.