

**Comparing Outcomes of Intrauterine Insemination in Stimulated Cycles Timed To HCG Trigger and Follicular Rupture: A Randomised Comparative Study**

<sup>1</sup>Dr Deepika Chahar, <sup>2</sup>Dr Jaya Choudhary, <sup>3</sup>Dr Jai Chowdhary, <sup>4</sup>Dr Pragya Choudhary

Department of Obstetrics and Gynaecology, Mahatma Gandhi Medical College & Hospital, Jaipur, Rajasthan, India.

**Corresponding Author:** Dr Deepika Chahar, Department of Obstetrics and Gynaecology, Mahatma Gandhi Medical College & Hospital, Jaipur, Rajasthan, India.

**Citation this Article:** Dr Deepika Chahar, Dr Jaya Choudhary, Dr Jai Chowdhary, Dr Pragya Choudhary, “Comparing Outcomes of Intrauterine Insemination in Stimulated Cycles Timed To HCG Trigger and Follicular Rupture: A Randomised Comparative Study”, IJMSIR- March - 2020, Vol – 5, Issue -2, P. No. 171 – 176.

**Type of Publication:** Original Research Article

**Conflicts of Interest:** Nil

**Abstract**

**Introduction:** Intrauterine insemination (IUI) is a well accepted treatment modality to improve pregnancy rates in infertile couples. It is a simple technique in which sperms are deposited into the uterus around the time of ovulation, thereby increasing the probability of fertilization and ensuing pregnancy. IUI can be performed with or without controlled ovarian hyperstimulation. Other factors which affect the pregnancy rates are age, duration of infertility, status of fallopian tubes, indication of IUI, timing and sperm preparation techniques.

**Aim & Objective:** To compare the pregnancy rates in patients undergoing IUI by timing IUI according to hCG trigger and follicular rupture.

**Method and Material:** A prospective hospital based study including 100 patients was conducted in Mahatma Gandhi Medical College and Hospital, Jaipur. Study included patients who fulfilled the inclusion criteria. 2 groups were made using computer- generated numbers- Group 1: IUI performed at 36-40 hours after HCG trigger and Group 2: IUI performed on the day of

follicle rupture confirmed by USG. Both groups were then subjected to various ovulation induction protocols and were monitored using serial ultrasonography following which IUI was done and luteal support was given accordingly.

**Result & Observation:** 47 patients were included in Group 1 and 53 were included in group 2. Out of 53 patients rupture occurred in 49 patients and rest 4 patients with no rupture with in 72 hours of HCG were excluded from the study. In my study mean age was 27.72 (group 1) and 27.55 (group 2), mean AFC was 9.06 (group 1) and 9.24 (group 2), mean baseline FSH was 5.67 (group 1) and 5.81 (group 2), mean duration of infertility was 4.27 (group 1) and 4.06 (group 2) and mean ET was 8.33 (group 1) and 8.07 (group 2) all of which were not significant statistically. The Overall pregnancy rate after IUI was 17.70% (17 out of 96). In Group 1 where IUI done after 36-40hr of HCG trigger pregnancy rate were 14.90% ( 7 out of 47) and in Group2 where IUI done after confirmation of rupture pregnancy rate were 20.40% (10 out of 49)which was slightly higher but not statistically significant.

**Conclusion:** IUI is a simple, cost-effective, non-invasive first-line therapy for cervical factor, anovulatory infertility, mild to moderate male factor, unexplained infertility and immunological infertility with clinical pregnancy rates ranging from 10 to 20%. IUI done after confirmation of follicle rupture does not increase pregnancy rate significantly. This could be because of low percentage of patient who had unruptured follicle (4 out of 53).

### **Introduction**

Intrauterine insemination (IUI) is a well accepted treatment modality to improve pregnancy rates in infertile couples. It is a simple technique in which sperms are deposited into the uterus around the time of ovulation, thereby increasing the probability of fertilization and ensuing pregnancy. It is less invasive and less expensive compared to in vitro fertilization, and therefore used as first line treatment for a variety of indications like mild to moderate male factor infertility, ovulatory dysfunction, minimal and mild endometriosis and unexplained infertility.<sup>1</sup>

IUI can be performed with or without controlled ovarian hyperstimulation, the reported success rates generally being higher in stimulated cycles compared to natural cycle.<sup>2</sup> Success rate of stimulated IUI varies between 7-20% per cycle.<sup>3,4</sup> certain variables affects IUI success and mostly related to the female partner like age, endometrial thickness, duration of infertility etc.<sup>5,6</sup> Other factors which affect the pregnancy rates are status of fallopian tubes, indication of IUI, timing and sperm preparation techniques.

Since spermatozoa and oocytes have only limited survival, timing the procedure correctly is a major determinant of successful outcome.

### **Aim & Objective**

To compare the pregnancy rates in patients undergoing IUI by timing IUI according to hCG trigger and follicular rupture.

### **Material and Methods**

A prospective hospital based study including 100 patients was conducted in Mahatma Gandhi Medical College and Hospital, Jaipur. Study included patients who fulfilled the inclusion criteria

### **Inclusion criteria**

- Age < 35yrs
- Unexplained infertility of < 7yrs
- Tubal patency (at least 1 tube patent)
- Sperm count > 10million/ml and 4% normal morphology on Kruger criteria
- Anovulation including PCOS

### **Exclusion criteria**

- Bilateral tubal block
- FSH >15mIU/ml
- Active genital tract infection
- Severe endometriosis
- Patient put on only injectable gonadotropins for stimulation

### **Ovulation induction protocol**

All couples fulfilling the eligibility criteria included in the study. All steps of study were explained to patients and informed written consent was taken.

Patients were randomized into 2 groups using computer-generated numbers.

Group 1: IUI performed at 36-40 hours after HCG trigger.

Group 2: IUI performed on the day of follicle rupture confirmed by USG.

Controlled ovarian stimulation given to all patients, either using oral ovulation inducing agents or combined

oral and gonadotropins, depending on patient profile. The different ovulation induction protocols, which used for stimulation, are as follows:

For induction we used oral ovulogen (Clomiphene citrate 50-100 mg or Letrozole 2.5-5 mg daily for five days starting on days 2-4 of the cycle) with or without gonadotropins FSH/HMG (75-150IU added on the day after the last oral dose and continued till the follicle is mature  $\geq 18\text{mm}$ ).

**Monitoring**

Baseline ultrasound done in all patients on Day 2-4 to exclude any residual cyst  $> 1\text{cm}$  and check endometrial thickness.

Serial transvaginal ultrasound performed starting the day after the last dose of clomiphene/Letrozole . Ultrasound repeated every alternate day until the follicle is 16 mm and then daily.

In both groups hCG injection 10,000 IU I.M. given between 9 to 10 pm when the follicle size is  $\geq 18\text{ mm}$ .

**Intrauterine insemination**

Group 1: IUI done 36-40 hours after hCG trigger i.e. between 10 am to 2 pm.

Group 2: Patients called for ultrasound daily at 10 am after hCG trigger given. IUI done on the day follicle rupture was documented, between 10 am to 2 pm but not beyond 72hours, Rupture of dominant follicle was confirmed on the basis of absence or shrinkage of dominant follicle with or without fluid in pouch of Douglas.

Semen preparation carried by double density gradient technique in all cases.

**Luteal support**

After insemination, luteal phase support given by oral dydrogesterone 10 mg twice daily for 14 days.

Pregnancy test (serum beta hCG) was done 14 days after the IUI. Ultrasound advised 2 weeks after the positive pregnancy test to document cardiac activity.

**Result & Observation-**

(A) Distribution of Groups- (Table 1)

IUI	Group 1	Group 2	Total
IUI done	47	49	96
IUI not done	Not applicable	4 (excluded from study)	4
Total patients included in study	47	49	

Table shows that total 100 patients were included, out of these 47 included in group 1 where IUI done after 36-40 hr of hCG trigger and 53 were included in group 2 where IUI has to be done after confirmation of rupture by USG. Out of 53 patients rupture occurred in 49 patients and rest 4 patients with no rupture with in 72hours of HCG were excluded from the study. (Table 1)

(B) Distribution of Patients According To Demographic Characteristics: (Table 2)

	GROUP 1			GROUP 2		
	Mean	Std deviation	P value	Mean	Std deviation	P value
Age	27.72	3.49	0.42	27.55	3.79	0.50
AFC	9.06	3.5	0.55	9.24	3.41	0.50
Baseline FSH	5.67	1.43	0.42	5.81	1.51	0.53
Duration of infertility	4.27	1.62	0.95	4.06	1.56	0.66
Endometrial thickness	8.33	1.44	0.53	8.07	1.42	0.50

In my study above table shows that in Group 1 the mean age of patients was 27.72 & std deviation was 3.49& p value was 0.42 , mean AFC was 9.06 & std deviation was 3.5& p value was 0.55, mean baseline FSH was 5.67 & std deviation was 1.43& p value was

0.42 , mean duration of infertility was 4.27 & std deviation was 1.62 & p value was 0.95, mean endometrial thickness was 8.33 & std deviation was 1.44 & p value was 0.53. (Table 2)

In Group 2 patients mean age was 27.55 & std deviation was 3.79 & p value was 0.50, mean AFC was 9.24 & std deviation was 3.41 & p value was 0.50, mean baseline FSH was 5.81 & std deviation was 1.51 & p value was 0.53 , mean duration of infertility was 4.06 & std deviation was 1.56 & p value was 0.66, mean endometrial thickness was 8.07 & std deviation was 1.42 & p value was 0.50. Result was not significant statistically. (Table 2)

(C) Distribution of Patients According To Indication of IUI (Table 3)

	GROUP 1		GROUP 2	
	Number	%	Number	%
Mild Oligoasthenozoospermia	9	19.15%	10	20.40%
Minimal & mild endometriosis	6	12.76%	6	12.25%
Anovulation	9	19.15%	11	22.45%
Unexplained infertility	21	44.68%	19	38.78%
Sexual dysfunction	2	4.26%	3	6.12%
Total	47	100%	49	100%
P value	0.97			

Above table shows that the indication of IUI in Group 1 out of 47 patients, 9(19.15%) had mild oligoasthenozoospermia , 6 (12.76%) had minimal to mild endometriosis , 9(19.15%) had anovulation ,21(44.68%) had unexplained infertility and 2(4.26%) had sexual dysfunction.(table-3) .

In Group 2 out of 49 patients 10 (20.40%) had mild Oligoasthenozoospermia , 6(12.25%) had minimal to mild endometriosis , 11(22.45%) had anovulation ,19(38.78%) had unexplained infertility and 3(6.12%) had sexual dysfunction .

However the difference was not significant statistically (p=0.97) (table-3)

Comparison Of Pregnancy Outcome In Patient Undergoing IUI Cycles According To Timed Hcg Trigger And Post Follicle Rupture In Both Groups.( Table 4)

Groups		Pregnant	Non pregnant	Total
Group 1(IUI done 36-40hr after HCG trigger)	Number	7	40	47
	%	14.90	85.10%	100%
Group 2 (IUI done after confirmation of rupture)	Number	10	39	49
	%	20.40%	79.60%	100%
P value	0.47			

Table shows that in Group 1 out of 47 patients 7(14.90%) were pregnant 40(85.10%) were not pregnant and in Group 2 out of 49 patients 10(20.40%) were pregnant 39(79.60%) were not pregnant. Overall, out of 96 patient with IUI 17(17.70%) were pregnant and 79(82.30%) were not pregnant. The difference in pregnancy rate was not significant statistically (p=0.47). (Table 4)

**Discussion**

Intrauterine insemination (IUI) is a well accepted treatment modality to improve pregnancy rates in infertile couples. There are various factors determining success of IUI cycle. Timing the IUI procedure correctly is one of the important determinant of successful outcome of procedure.

When both the Groups were compared according to the timing of IUI on the basis of follicle rupture after the trigger we found that Group 2 where IUI was done only after confirmation of rupture of follicle, showed a better pregnancy rate in comparison to patients in Group 1 where IUI was done after 36-40 hr of HCG trigger irrespective of rupture of follicle. (PR in Group 1 was 14.90% and in Group 2 was 20.40%). Although no statistically significant difference was found (P value =0.47) among both the Groups but our study showed a better outcome where follicle rupture was confirmed before IUI.

Similar to our study Tansu Kucuk et al also found that Clinical pregnancy rate was 23.5% (64/272) in the group when follicle rupture was evident by transvaginal USG, while it was only 8.8% (27/306) when follicle rupture was not evident ( $p < 0.001$ ).

In their study they have explained the incidence of luteinized unruptured follicle syndrome (LUF) has been reported to be 10% among fertile women. It is reported to be as high as 25% in unexplained infertile couples undergoing IUI with Clomiphene Citrate . LUF decreases the chance of pregnancy after intrauterine insemination treatment. Ultrasound has been demonstrated to be the method of choice for diagnosis of LUF . Postponement of IUI until demonstration of follicular rupture will avoid insemination in the presence of LUF and such a strategy may increase the pregnancy rate per inseminated cycle with IUI treatment.<sup>(7)</sup>

### Conclusion

IUI is a simple, cost-effective, non-invasive first-line therapy for cervical factor, anovulatory infertility, mild to moderate male factor, unexplained infertility, and immunological infertility with clinical pregnancy rates ranging from 10 to 20%.

Controlled ovarian hyperstimulation can be combined with IUI to obtain the adequate number of follicles and thereby increasing the success rate. Among the various factors affecting the success rate of an IUI cycle one important determinant is timing of IUI, either according to the HCG trigger or after confirmation of rupture of follicle.

In Our study we compared the difference in clinical pregnancy rates when IUI was done at a fixed interval after the HCG injection i.e. 36-40hr or after documenting follicle rupture .

Our study concluded that although there was no statistically significant difference found but clinical pregnancy rate was better in group where follicle rupture was confirmed by USG before performing IUI in comparison to the group where follicle rupture was not confirmed.

### References

1. Zegers-Hochschild F, Adamson GD, de Mouzon J, Ishihara O, Mansour R, Nygren K, et al. The (ICMART) and the (WHO) 2009. Hum Reprod. 2009;24:2683–2687.[PubMed] (Firouzeh Ghaffari M.D., Arezoo Arabipoor M.Sc et all jan 2018)
2. Thoma ME, McLain AC, Louis JF, King RB, Trumble AC, Sundaram R, Buck Louis GM Fertil Steril. 2013 Apr; 99(5):1324-1331.e1. [PubMed] .
3. Kovac JR, Pastuszak AW, Lamb DJ ,The use of genomics, proteomics, and metabolomics in identifying biomarkers of male infertility. Fertil Steril. 2013 Mar 15; 99(4):998-1007. [PubMed]
4. Sarapan Na Nakhon, Pawan Limvorapitux, and Patsama Vichinsartvichai Knowledge regarding factors that influence fertility in Thai reproductive-age population living in urban area: A cross-sectional study”. Clin Exp Reprod Med. 2018

Mar; 45(1): 38–43. Published online 2018 Mar 30. doi: 10.5653/cerm.2018.45.1.38

5. Tomlinson MJ , Amissah-Arthur JB , Thompson KA , Kasraie JL , Bentick B Infertility : Prognostic indicators for IUI success: Statistical model for IUI success. *Human Reproduction* , 1996; 11(9) : 1892-1896.
6. Badawy A, Elnashar A, Eltotongy M. Effect of sperm morphology and number on success of intrauterine insemination. *Fertil Steril*. 2009;91:777–781. [PubMed].
7. Tansu Kucuk “Intrauterine insemination : is the timing correct?” *J Assist Repord Genet*.2008 Aug ;25(8):427-430