

## COMPARISON OF HCG TRIGGERED OVULATION VERSUS NATURAL OVULATION ON PREGNANCY OUTCOME IN DONOR INTRAUTERINE INSEMINATION

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### Abstract

**Background:** To evaluate the effect of Human Chorionic Gonadotropin (HCG) triggered ovulation versus natural ovulation on pregnancy outcome in donor intrauterine insemination (IUI-D) cycles. **Materials and Methods:** This study was performed during the period of January 2015 to January 2021 in ART Clinic of Obstetrics & Gynecology Department at Shri Guru Ram Rai Institute of Medical & Health Sciences Dehradun. It was a Retrospective cohort study which was done on 290 patients of primary infertility treated with donor IUI. In 145 patients, HCG injection was used for triggering ovulation in intra uterine insemination donor patients (group A), and in 145 patients natural ovulation was allowed to occur (group B). Transvaginal Ultrasound was used to detect ovulation in both the groups. Both the groups were observed for results in terms of positive clinical pregnancy test and live birth rates. **Result:** Positive pregnancy test was observed in 27.59 % patients in Group A Vs 17.93 % in Group B. Live birth rate was observed in 24.83 % in Group A vs 15.86 % in Group B (P value was higher for HCG triggered group A than for spontaneous ovulation group B). Reproductive outcomes were statistically better for HCG triggered group. **Conclusion:** In IUI patients, HCG triggered ovulation offers better results than spontaneous ovulation in terms of positive clinical pregnancy test and live birth rate.

## INTRODUCTION

Donor Intrauterine insemination (IUI - D) is a low budget procedure with minimal invasion. IUI (D) involves timely insemination of donor sperms into the uterine cavity in stimulated or natural cycles. Timing of insemination is one of the most important factor influencing the success rate of IUI (D).<sup>2</sup> Various methods are used for timing IUI (D). One of the most accepted methods for timing ovulation is use of HCG Injection. It not only requires less monitoring but also has an effect on endometrial receptivity.<sup>[1]</sup> This study examined a cohort of women undergoing minimally stimulated IUI (D) cycles. The objective of the study was to evaluate the effect of HCG triggered ovulation versus natural ovulation on pregnancy outcome in donor Intra uterine insemination cycles.

## MATERIALS AND METHODS

This study was conducted between January 2015 to January 2021 in ART Clinic of Obstetrics & Gynecology Department at Shri Guru Ram Rai Institute of medical and health sciences Dehradun. It is a retrospective study which included those patients who came for infertility treatment and required IUI (Donor). Prior to IUI cycles, basic infertility workup of all women was performed which included Day 2- FSH, LH, Estradiol, Anti Mullerian hormone (AMH), S. Prolactin and thyroid stimulating hormone levels. Tubal patency of at least one fallopian tube was ensured in advance prior to planned IUI. A transvaginal ultrasound for anatomy and follicular monitoring was also done. Patient selection criteria was - age less than 35 years, regular menstrual cycle, no history of medical condition likely to cause infertility, normal baseline hormonal status and at least one patent fallopian tube. Exclusion criteria was - age more than

35years, irregular cycles, tubal factor infertility, PCOS (According to Rotterdam ESHRE/ASRM-PCOS consensus workshop Group 2004), Abnormal TSH or Prolactin or any known metabolic endocrinological disease. Women with incomplete records were excluded from the study. Patients were divided into two groups A and B. After a baseline Day-2 scan, Tab Letrozole 2.5 mg once daily was started on 2<sup>nd</sup> or 3<sup>rd</sup> day for 5 days for ovulation induction in both the groups. A serial USG for Follicular monitoring was started from day 9 in all patients. In Group A, when dominant follicle was of size 18-20 mm, ovulation was triggered with the help of injection Human Chorionic Gonadotropin 5000 IU given intramuscularly at night (between 8 to 9 p.m.) and IUI(D) performed after 36 hours. In group B, natural ovulation was allowed to occur and IUI(D) was done on the day of spontaneous ovulation. Ovulation was confirmed by TVS in both the groups before performing IUI with donor sample. The choice to use HCG trigger along with USG monitoring or only USG monitoring was made according to the patient's preference. Frozen Donor semens were obtained from Cryobank India New Delhi and were thawed before the IUI procedure. Quantity and quality of sperm were evaluated before each IUI(D). Simple wash was performed with each frozen semen sample. Only Samples with sperm count more than 30 million per ml and grade A motility more than 60% were used. In both the groups Insemination was performed in IUI procedure room using sperm launcher soft IUI cannula and 0.5 ml of semen was used for each IUI (D). Bed rest was maintained for 30 minutes after IUI insemination, serum beta HCG was performed on 15<sup>th</sup> day of IUI. Transvaginal USG was performed after 15 days of positive Beta HCG test to look for localization, viability, number of Gestational sacs and any other significant findings.

**Data Analysis:** Pregnancy was confirmed positive when Beta HCG value were more than 25 m IU/ml after 15 days of IUI and fetal viability was confirmed by TVS after 15 days of positive serum Beta HCG. Live birth was defined as delivery of a neonate after 28 weeks of gestation. Our primary outcome was clinical pregnancy rate and secondary outcome was live birth rate. Statistical analysis was performed using SPSS Statistics software 20.0 version. Mean value and standard deviations were calculated for each continuous variables. Students-t test and chi-squared test were used for comparison.

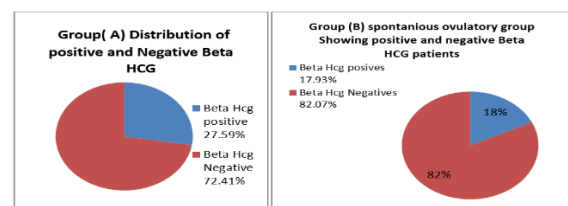
P value <0.05 was considered statistically significant.

## RESULTS

A total number of 290 patients were treated with IUI (D) from Jan 2015 to Jan 2021. Baseline Characteristics & hormonal profile of the patients in Group A & Group B were noted and analyzed in Table 1. No statistically significant differences were noted among BMI, AMH or Estradiol levels between patient of the two groups, while slight differences were detected in age and basal FSH and LH concentration but these differences were not statistically significant.

Primary outcome in the form of positive pregnancy test outcome in group A and B are shown in observation Table-2 and Figure 1. In group A out of 145 patients, pregnancy test was positive in 40 patients (27.59 %). Negative pregnancy test was found in 105 patients (72.41 %). In group B out of 145 patients clinical pregnancy test was positive in 26 patients (17.93 %). Whereas in 119 (82.07 %) patients pregnancy test was negative. The difference in primary outcome (positive pregnancy test) between the two groups was statistically significant (P value < 0.05).

Secondary outcome in the form of Live births in both the groups are shown in Table-3 and Figure 2. In group A, 36 patients (24.83 %) out of 145 had live births. Four (2.75 %) had pregnancy failure after initial positive pregnancy test. In group B, 23 patients (15.86 %) out of 145 had live births. Three (2.07%) patients had pregnancy failure after initial positive pregnancy test. The difference in secondary outcome (live birth rate) between the two groups was statistically significant (p value <0.05). Overall results of Group A were better than group B and the difference was statistically significant (p value <0.05.)



**Figure 1: Pregnancy test results in group A and group B**

**Table 1: Demographic characteristics of the patients**

GROUPS	Group A (145 patients) HCG Triggered ovulation	Group B (145 patients) Spontaneous Ovulation	P value
Age	27.22±3.40	22.12±3.20	0.013
BMI	22.13±3.11	22.12±3.14	0.853
AMH	4.22±2.80	4.18±2.83	0.53
FSH(IU/L)	6.62±1.67	6.82±1.32	0.001
LH(Miu/l)	4.44±2.36	5.08±2.11	0.011
Estradiol(pg/ml)	34.75±13.11	34.22±12.62	0.615
Endometrial thickness on the day of insemination (cms)	1.02±0.11	1.01±0.13	0.06

**Table 2: Comparison of positive Beta HCG in group A and B**

Groups	Beta HCG >25.0 mIU/ml Pregnancy positive	Beta HCG <25.0 mIU/ml Pregnancy negative
Group A (HCG)	40 (27.59 %)	105 (72.41 % )
Group B (Spontaneous ovulation )	26 (17.93 % )	119 (82.07 %)
Total	66	224

Chi square = 6.5

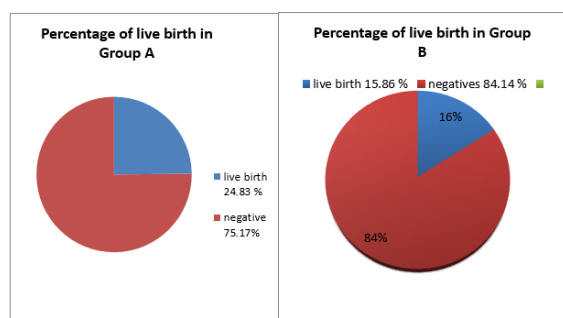
P value < 0.05(significant)

**Table 3: Comparison of Live births in Group A and Group B**

Name of group	Live births	No. of abortions
Group A (HCG triggered ovulation)	36 (24.83 %)	(75.17%)
Group B (Spontaneous ovulation)	23 (15.86 %)	(84.14%)
Total	59	

Chi Square=5.1

P Value<0.05 (significant)

**Figure 2: Live birth rate in Group A & B**

## DISCUSSION

Present study shows that administration of Injection HCG for triggering ovulation was more successful than spontaneous ovulation group in donor IUI in controlled stimulation Group. Ji-Peng Wan et al studied effect of HCG-Triggered Ovulation on Pregnancy outcomes in Intrauterine Insemination: An Analysis of 5,610 First IUI Natural Cycles with donor sperm in China was done. This study concluded that HCG triggered ovulation for timing insemination offers beneficial impacts on both clinical pregnancy rates and live birth rates.<sup>[1]</sup> Ji-Peng Wan et al found that clinical pregnancy rate was 27.40% after HCG administration and 22.73% after spontaneous ovulation which is comparable to our study (27.59% after HCG administration and 17.93 % after spontaneous ovulation) though the sample size of present study was small. Previous studies have established that the success of IUI depends on various factors like age of female, sperm quality, type of subfertility, ovarian stimulation and timing of insemination.<sup>[2]</sup> Spermatozoa and ovum both have limited short survival duration, the accurate timing of IUI relative to ovulation may be one of the most important factor influencing the IUI success rate.<sup>[2]</sup> Many studies on ovarian stimulation in IUI Cycle have demonstrated beneficial effects of HCG administration on IUI pregnancies .Study by Taerk et al reported that Injection HCG administration significantly increased clinical pregnancy rates when compared with monitoring of spontaneous serum LH surge in sub fertile patients

undergoing controlled ovarian hyper stimulation IUI cycles.<sup>[3]</sup> When HCG was given along with a serum LH surge clinical pregnancy rates were found to be the highest. Their study emphasized the importance of HCG trigger and timing of IUI. The results of this study are also comparable to our study. Cochrane meta-analysis by Cantineau et al compared different technique of timing for IUI. Ten studies were included in this metaanalysis comparing urinary LH surge with HCG. Outcome analysed showed no significant differences between the two groups.<sup>[4]</sup> Our study results are not comparable with this study. The reason may be that in our study follicular monitoring for identifying ovulation was done by the same Gynecologist who performed IUI. Razieh Deghani-Firouzabai et al compared the fertility rates in an IUI protocol in women who took an HCG injection before and after the IUI. The pregnancy rates were 10 and 12 % (P = 0.85), respectively. They concluded that HCG administration after IUI brought about no improvement in the pregnancy rate. Therefore, HCG can be administered either before or after IUI. But their study did not have comparison with patients without HCG administration.<sup>[5]</sup> Ioannis P Kosmas et al has investigated the pregnancy outcome of HCG administration for triggering ovulation in a natural cycle IUI.<sup>[6]</sup> This study was a Meta-analysis of prospective and retrospective trials. The meta-analysis included all controlled trials examining the effectiveness of HCG administration before IUI on clinical-pregnancy rates in comparison with LH detection. Patients who received HCG before IUI demonstrated lower clinical pregnancy rates then did women who had IUI after spontaneous ovulation which is in contrast to our findings. Plosker et al analysed 381 consecutive cycles of homologous intra-uterine insemination (IUI) in 215 infertile couples and found that cycles in which pre-ovulatory surges were either induced or supported with human chorionic gonadotrophin (HCG) were superior to spontaneous luteinizing hormone surges (0.13 versus 0.03, P = 0.05) as seen in our study. They recommended that stimulation protocols and mid-cycle HCG are necessary to achieve an acceptable pregnancy rate.<sup>[7]</sup> Inclusion criteria of our

study was strict and only normo-ovulatory women aged <35 years of age who underwent IUI with high quality donor sperm included which enabled analysis of a well-defined cohort of women with no obvious confounding factors. Another strength of our study is that transvaginal USG for measuring the follicular size and detecting ovulation was done by the gynecologist in gynecology department only. Outcome measures included not only the clinical pregnancy rate but also the live birth rate.

## CONCLUSION

In donor IUI patients, the administration of HCG for triggering ovulation is significantly better than spontaneous ovulation in terms of positive clinical pregnancy test and live birth rate.

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