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Original Research Article

Association between trigger-intrauterine insemination interval, ovulation trigger agent, and clinical pregnancy in intrauterine insemination cycles: a 300-case analysis

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ABSTRACT

Background: Intrauterine insemination (IUI) is a commonly employed first-line treatment for couples with unexplained infertility and mild male factor infertility due to its simplicity, low cost, and minimal invasiveness. Ovulation is typically induced using pharmacological triggers to allow accurate scheduling of IUI either with human chorionic gonadotropin (hCG) or gonadotropin-releasing hormone (GnRH) agonists. While insemination is commonly performed between 24 and 40 hours after the trigger, studies have reported variable pregnancy rates across different timing intervals, and no universal consensus has been established. Given these uncertainties, further evaluation of both the timing of insemination and the choice of ovulation trigger is warranted. Hence this study aims to assess how the interval between ovulation trigger and IUI influences clinical pregnancy outcomes, and to compare pregnancy rates between cycles using a GnRH agonist versus hCG as the trigger.

Methods: A retrospective analysis was conducted on 300 IUI cycles performed at Janani Fertility Centre, Trichy, Tamil Nadu. Eligible cases included couples with unexplained infertility, male partners aged 23–40 years, and female partners aged 22–38 years with bilaterally patent fallopian tubes. Cycles with abnormal semen parameters, incomplete or frozen samples, double IUI, or donor sperm use were excluded. Patients were grouped according to the interval between trigger administration and IUI: <36 hours (group A, n=70), 36–38 hours (group B, n=140), and >38 hours (group C, n=90). Trigger type was hCG (n=187) or GnRH agonist (n=113). Categorical variables were analyzed using the Chi-square test.

Results: Clinical pregnancy rates differed significantly across timing groups: group A: 8.6%, group B: 25.7%, and group C: 15.6%. The highest pregnancy rate occurred when IUI was performed 36–38 hours after the ovulation trigger. Trigger comparison showed higher pregnancy rates with hCG (25%; 47/187) than with GnRH agonist (8%; 9/113).

Conclusions: IUI performed 36–38 hours after ovulation trigger is associated with the highest likelihood of clinical pregnancy, indicating optimal synchronization of ovulation and insemination at this interval. Additionally, hCG appears more effective than GnRH agonist as a trigger for improving pregnancy outcomes in IUI cycles.

Keywords: IUI, Ovulation trigger, Insemination interval

INTRODUCTION

Infertility is clinically characterized as the inability to conceive after 12 months of regular, unprotected intercourse, and when a routine evaluation fails to identify any underlying causes the condition is classified as unexplained infertility.[1] Intrauterine insemination (IUI) continues to be a commonly utilized assisted reproductive treatment for couples with unexplained infertility, mild male factor infertility, or certain ovulatory disturbances.[2]

It represents a less invasive and more economical alternative to IVF, while still providing favorable success rates when appropriately timed and when suitable patient selection criteria are applied. Among the various determinants of IUI success, the interval between the ovulation trigger and insemination is one of the most critical factors.[3]

Ovulation induction is usually achieved with either human chorionic gonadotropin (hCG) at a standard dose of 10,000 IU or a gonadotropin-releasing hormone (GnRH) agonist. While hCG functions by emulating the natural LH surge, a GnRH agonist initiates an endogenous LH surge that more closely replicates physiological ovulation.[4] The choice between these agents influences the timing of follicular rupture and the synchronization between ovulation and insemination, thereby potentially impacting fertilization success.

The interval between trigger administration and IUI has been widely investigated, as it plays a pivotal role in optimizing cycle outcomes. Current recommendations generally advise performing IUI within 24–36 hours after administering the ovulation trigger, typically hCG.[5] The most favorable pregnancy outcomes have been reported when insemination takes place 32–38 hours after hCG injection, coinciding with the timeframe in which oocyte demonstrates its highest fertilization potential and sperm remain viable within the female reproductive tract.[6,7]

While IUI success appears largely independent of insemination technique or sperm preparation method, guidelines suggest using the processed sample within about one hour of preparation.[8,9] Some clinical protocols provide broader flexibility, permitting insemination up to six hours before or after the anticipated time of ovulation.[10,11] Double IUI cycles—performed both before and after ovulation—have also been explored, though a single, well-timed insemination is still considered the standard of care.

Aim and objectives

Primary objective of the study was to assess the clinical pregnancy rate based on different time intervals between ovulation trigger and IUI. Secondary objective of the study was to compare pregnancy outcomes following the use of GnRH agonist versus hCG 10000 IU as ovulation triggers in IUI cycles regardless of the trigger-to-IUI interval.

METHODS

This retrospective study analyzed records of 300 patients who underwent IUI at Janani Fertility Centre, Trichy, Tamil Nadu, from June 2023 to August 2025.

Inclusion criteria

Inclusion criteria comprised couples with male partners aged 22–40 years and female partners aged 22–38 years undergoing IUI treatment with bilateral tubal patency and post-wash sperm count greater than 10 million/ml.

Exclusion criteria

Exclusion criteria consisted of severe male factor like low sperm count (<5 million/ml), incomplete or frozen semen samples, severe Endometriosis, cycles involving double IUI, and the use of donor semen.

Ovarian stimulation was performed using either clomiphene citrate or letrozole, administered from day 2 of the menstrual cycle for five consecutive days along with or without gonadotrophins. Follicular growth was monitored using transvaginal ultrasonography till the development of dominant follicle, and cycles were cancelled if more than three dominant follicles developed. An ovulation trigger was administered when the dominant follicle measured between 20 and 22 mm in diameter. Either a GnRH agonist (inj. Lupride 1 mg) or hCG 10000 IU was administered sub cutaneously for ovulation triggering, in accordance with evidence showing equivalent efficacy and pregnancy outcomes for both agents.

For the IUI procedure, semen was collected in a sterile container, the collected semen was processed immediately after liquefaction by double density gradient (500 g for 15 minutes followed by 300 g for 10 minutes) and allow to swim-up (40 minutes) to concentrate the motile sperm and remove debris. About 0.5 ml of the processed semen was loaded into a catheter immediately after preparation and slowly injected into the uterine cavity while the woman was in a lithotomy position. After insemination, the woman was positioned in a supine position for 15 minutes to facilitate sperm migration. For luteal support capsule progesterone 300 mg is given vaginally for 14 days for all the women irrespective of the group they belong.

The interval between trigger administration and IUI was determined by factors including male partner availability, patient and hospital convenience. Participants were divided into three groups according to this interval: group A: IUI performed less than 36 hours after trigger (n=70), group B: IUI performed between 36 and 38 hours after trigger (n=140) and group C: IUI performed more than 38 hours after trigger (n=90).

The collected data were entered in the Microsoft Excel 2016 and analysed with IBM statistical package for the social sciences (SPSS) statistics for Windows, Version 29.0. (Armonk, NY: IBM Corp). To describe about the data descriptive statistics frequency analysis, percentage analysis was used for categorical variables and the mean and standard deviation were used for continuous variables. To find the significant difference in the multivariate analysis the one-way ANOVA was used.

To find the significance in qualitative categorical data Chi-square test was used similarly if the expected cell

frequency is less than 5 in 2×2 tables then the Fisher's Exact was used. In all the above statistical tools the probability value 0.05 is considered as significant level.

RESULTS

All the data were collected from the clinical records of the patients who fulfilled the above-mentioned inclusion criteria.

Table 1 shows the demographic factors and cycle characteristics of the study population.

Table 1: Demographic and baseline characteristics of the study population.

Parameters	Overall baseline (mean±SD)
Maternal age (years)	25.5±4.0
Paternal age (years)	35.0±5.0
Number of follicles stimulated	1.87±0.24
Endometrial thickness (mm)	8.35±2.21
Post-wash sperm count (million/ml)	37.3±28.3

The study population were divided into the following groups based on the interval of insemination is shown in Figure 1.

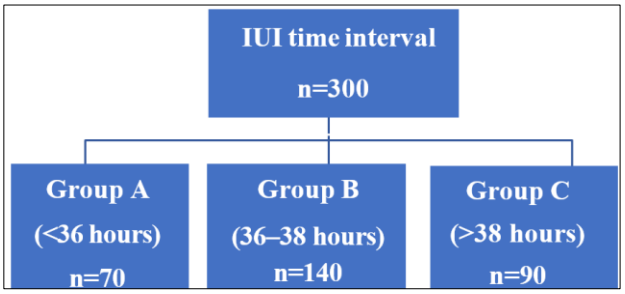

Figure 1: The distribution of the study population based on the time interval between the trigger and IUI.

Among 300 subjects, 187 received hCG trigger and 113 received GnRH agonist trigger (Figure 2).

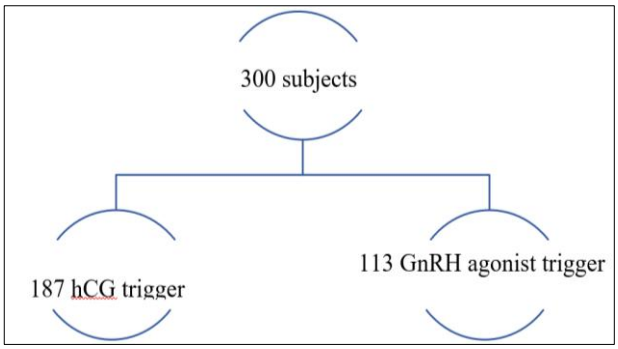

Figure 2: Distribution of study population between different trigger agent (hCG and GnRH agonist).

The distribution of the study population based on the time interval between the trigger and IUI illustrated in Figures 1 and 2. Table 2 shows the key factors that influence the success rates of IUI-such as the age of both female and male partners, endometrial thickness, the number of follicles stimulated, and the post-wash semen parameters. When one -way ANOVA was used p value was found to be non-significant (no statistical significance at p>0.05).

Figure 3 shows the positive outcome percentages for each group, with group B having the highest at 25.7%, followed by group C at 15.6%, and group A at 8.6%. The Chi-square test for these positive outcomes only yielded a p=0.007 (p<0.05), indicating statistically significant difference between the groups.

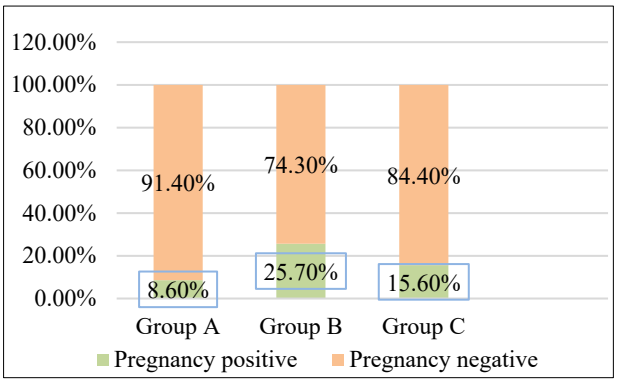

Figure 3: Pregnancy outcome between the groups based on insemination interval.

Table 2: Comparison of baseline characteristic between the study group

Baseline characteristics	Group A (n=70)	Group B (n=140)	Group C (n=90)
Maternal age (years)	27±4.3	25±4	25±3.6
Paternal age (years)	39±5.4	35±4	32±3.9
Number of follicles stimulated (mm)	1.9±0.2	1.9±0.2	1.8±0.3
Endometrial thickness (mm)	8.3±2.3	8.4±2.3	8.3±2
Post wash count (million/ml)	33.8±23.2	36.3±30.5	41.5±28.1

When focusing only on positive outcomes, the hCG 10000 IU group had a positive outcome rate of 25.1%, while the GnRH agonist group showed 7.9%. However, a Chi-square test gave a p value of 0.339, which is not statistically significant. This means that, even though the hCG group appears to perform better, the difference could

merely be due to random variation and not a real effect of the trigger injection type (Figure 4).

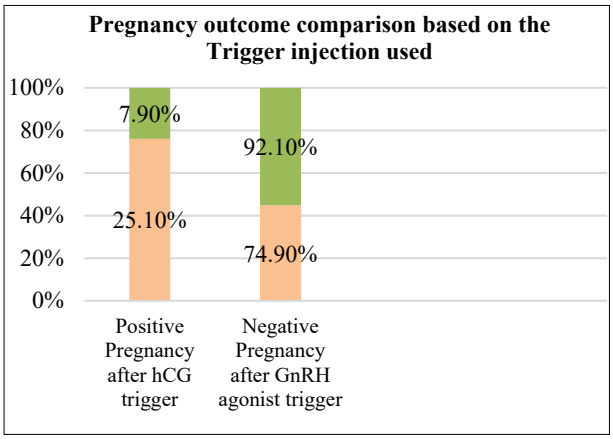

Figure 4: Outcome between hCG and GnRH agonist trigger injection.

DISCUSSION

While international studies report IUI success rates averaging 9-11%, our study achieved a higher clinical pregnancy rate of 18.7%. A review of ASRM guidelines shows that the recommended first-line treatment for unexplained infertility is ovarian stimulation with oral medications and intrauterine insemination (over three or four cycles.[10] This study specifically analyzed how the timing between the ovulation trigger and IUI affects success. Consistent with a Cochrane review and other literature, no significant difference was found in pregnancy rates when IUI was done between 24- and 48-hours post hCG trigger administration.[5,12,13]

Studies comparing IUI performed simultaneously with the ovulation trigger and IUI conducted 34–36 hours after the trigger have found no significant differences in clinical pregnancy rates between the two approaches.[14]

Some studies have shown that clinical pregnancy rates tend to be higher when IUI is performed 36 hours after the ovulation trigger, though this increase is not always statistically significant.[15] Conversely, other research points to a higher pregnancy incidence when IUI is done immediately after hCG trigger administration compared to insemination at 24–32 hours post-trigger.[16] Differences in findings may arise from variations in patient groups, clinical protocols, and other influencing factors. Since fertilization success depends on timing the insemination close to ovulation, variations within this window could impact outcomes differently.

The oocyte has a relatively brief lifespan after ovulation, while spermatozoa can survive for a longer duration within the female reproductive system. Because of this, it is essential for sperm to be present when the oocyte is released to maximize the chances of fertilization. The extended viability of sperm ensures they can wait for the oocyte, increasing the likelihood of successful sperm-oocyte interaction during this critical timeframe.

Using a GnRH agonist (GnRHa) to trigger ovulation can negatively affect the luteal phase and the receptivity of the endometrium.[17] This trigger causes the body to release its own luteinizing hormone (LH), which remains active for about 60 minutes, significantly shorter than the approximately 24-hour duration of hCG.[18] Because hCG lasts longer, it prompts the continued release of substances that increase blood vessel permeability, raising the risk of ovarian hyperstimulation syndrome (OHSS). In contrast, the shorter activity span of LH after GnRHa administration reduces stimulation of the corpus luteum, resulting in lower levels of estradiol and progesterone, thus lowering the chance of OHSS compared to triggers using hCG.[19] Another study showed that the dual trigger combination of GnRH-a and recombinant hCG significantly improves the outcome of intrauterine insemination.[20] No statistical significance observed between hCG and GnRH agonist trigger in our study.

Limitations and strengths

This study is strengthened by a relatively large sample size and strict inclusion and exclusion criteria, which reduced confounding factors related to semen quality and tubal status. Conducting all cycles at a single center ensured consistent clinical protocols, and grouping cases by specific trigger-to-insemination intervals enabled focused assessment of optimal timing. The comparison between hCG and GnRH agonist triggers also adds practical clinical relevance.

Limitations include the retrospective, single-center design, which may introduce bias and limit generalizability. Lack of randomization for trigger type and insemination timing, along with unaccounted variations in drugs used for stimulation, may have influenced outcomes. Additionally, only clinical pregnancy rates were analyzed, without evaluation of live birth rates or other contributing cycle parameters

CONCLUSION

In our study, we observed higher pregnancy rates when IUI was performed 36–38 hours after either hCG or GnRH agonist trigger, aligning with the ovulation window and implantation timing. While hCG triggers yielded higher pregnancy rates overall, GnRH agonist can be used as a safe alternative, especially in cases with more than three dominant follicles, to reduce the risk of ovarian hyperstimulation.

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